JPRS 75654

8 May 1980

USSR Report

SPACE BIOLOGY AND AEROSPACE MEDICINE

Vol. 14, No. 2, 1980

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USSR REPORT

Space Biology and Aerospace Medicine

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Translation of the Russian-language monthly journal KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA published in Moscow by the Meditsina Izdatel'stvo.

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PUBLICATION DATA

English title	:	SPACE BIOLOGY AND AEROSPACE MEDICINE, Vol 14, No 2, 1980
Russian title	:	KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA, Vol 14, No 4, 1980
Editor	:	O. G. Gazenko
Publishing house	:	Meditsina
Place of publication	:	Moscow
Date of publication	:	March-April 1980
Signed to press	:	11 February 1980
Copies	:	1755
COPYRIGHT	:	Kosmicheskaya biologiya i aviakosmicheskaya meditsina, 1980

SURVEYS

UDC: 612.2.014.41

RESPIRATION AND GAS EXCHANGE UNDER HYPERBARIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 3-10

[Article by L. A. Bryantseva, I. S. Breslav and A. G. Dianov, submitted 16 Jan 78]

[English abstract from source]

The paper reviews the data available on the respiratory effects of the breathing gas increased density, which include respiratory mechanics, pulmonary ventilation, and oxygen and carbon dioxide transport. Particular attention is given to the respiratory system as a limiting factor for human performance in a hyperbaric environment. The paper discusses optimization of gas mixtures used in undersea dives.

[Text] One of the tasks confronting physiology and medicine related to exploration of the resources of the oceans is to assure not only normal vital functions but high efficiency of man while under water. This requires comprehensive studies of the effects of a hyperbaric environment on respiratory function, since high pressure and, consequently, increased density of the gas environment are factors that affect primarily respiration and exchange of gases in the body. While the maximum tolerated muscular load under ordinary conditions depends on the reserves of the circulatory system, in the case of deep dives wearing diving gear or in an underwater habitat the respiratory system plays the limiting role. S. Miles states that "physiology of respiration is the key to submarine medicine" [1].

In this survey we shall discuss current data on the effects of a hyperbaric environment on respiration and gas exchange, without touching upon such questions as the effects of high pressure neutral gases on the central nervous systems, changes in heat transfer, effects of hyperoxia, decompression disorders, etc.

Most often the effects of hyperbaric conditions are studied with the use of high pressure chambers [2-14] rather than during actual submersion (which involves methodological difficulties). Another method that has

become popular more recently involves simulation of the hyperbaric factor by means of mixtures of O_2 and "heavy" gases--Ar, Xe and Sf --and the respiratory reactions to such high density mixtures turned out to be identical to the respiratory changes in a hyperbaric environment [5, 15-29]. Table 1 lists the results of our estimates, which indicate the depths that are equivalent in density to mixtures of different gases and O_2 at normal partial oxygen pressure.

Table 1. Densities of various inert gases and normoxic mixtures thereof

Parameter	Inert gases							
	N_2	H_2	He	Ne	Ar	Kr	Xe	SF_6
Gas density, g/ℓ	1,25	0,09	0,18	0,90	1,78	3,74	5,89	6,50
Relative gas density (air density is considered to be 1)	0,97	0,07	0,14	0,70	1,38	2,87	4,52	5,03
Relative density of normoxic mixture (air density taken as 1)	1,00	0,29	0,31	0,78	1,32	2,52	3,84	4,21
Depth equivalent in density to given mixture, m water column*	0	-	--		3	16	29	33

*Depth estimates were made with consideration of decline in fractional O_2 level required to maintain at a given depth a pO_2 of 0.21 kgf/cm^2.

The first link in the chain of changes due to high atmospheric density is an increase in resistance to gas flow in the airways. It can increase even more due to the breathing gear used in diving. S. Miles describes the sensations of a diver as follows: "You do not breathe, but suck air in, then forcefully blow it out" [1]. This factor can be simulated to some extent by using an artificial resistive (nonelastic) resistance to respiration, for example, by connecting a narrow hose or perforated diaphragm to the breathing valve [30-34]. Examination of patients with obstructive lesions to the respiratory system also yields information about the effects of increased resistance to air flow [35, 36].

As we know, resistance to gas flow in the tracheobronchial tress is attributable to the properties of inhaled gas, as well as nature and rate of flow. In a hyperbaric atmosphere, there is an increased tendency toward changing from laminar to turbulent flow. At pressures of 5-6 kgf/cm^2,*

*We refer here and elsewhere (unless otherwise indicated) to a normoxic nitrogen-oxygen environment.

virtually all of the gas flow in the airways becomes turbulent [9, 37]. Gas density acquires decisive significance to level of resistance. Other conditions being equal, the resistance to respiration increases with increase in ambient pressure, proportionately to the square root of gas environment density [38]. At the same time, according to the equation of Rohrer, the resistance to turbulent flow is proportionate to the root of the velocity of this flow. For this reason, there is an increase in energy expended by man for the function of respiratory muscles [2, 10, 21, 31, 39] and appearance of the sensation of dyspnea [40, 41] under hyperbaric conditions.

The increase in resistance to respiration leads to slowing of maximum inspiratory and, particularly, expiratory flow in the airways [4, 41-44]. The change in magnitude of peak expiratory flow is inversely related to density of the environment or, more precisely, it is proportionate to density to the power of -0.41 or -0.45 [8, 14].

With increase in density of the environment, the magnitude of expiratory flow is limited by the following phenomenon: when intrathoracic pressure reaches a critical level during forced (due to increased resistance) expiration the small bronchi collapse. Further increase in expiratory effort becomes ineffective and can no longer cause emptying of alveolar spaces [26, 45].

In view of the limited velocities of gas flow in the airways there is a decrease in maximum breathing capacity (MBC). The change in this parameter is directly related to the increase in resistance to air flow and, consequently, inversely proportionate to the square root of gas environment density [1, 8, 26, 27, 42 and 46]. One can predict the MBC at different depths on the basis of this pattern. These estimates are listed in Table 2. It is easy to see that the decrease in MBC slows down with increase in pressure. At the same time, the MBC values are somewhat higher in actuality than the estimates [1, 43, 47]. The increased effort developed by respiratory muscles with increase in resistance to gas flow may be one explanation for this.

Indeed, increased resistance to respiration induces several reflex reactions of an adaptive nature. There is an increase in activity of respiratory motoneurons and force of contraction of respiratory muscles [33, 36, 39, 48]. Respiration becomes slower and deeper; slowing of gas flow makes it possible to overcome the resistive resistance with less expenditure of energy [5, 6, 18, 49-52].

However, these reactions compensate only partially for the effect of the increased load on the respiratory system. The observed decrease in MBC inevitably leads to limitation of efficiency [work fitness] [47, 53]. For the body cannot perform the heavy muscular work, which requires increased pulmonary ventilation in excess of the level that is the maximum under such conditions, for a long period of time. In actuality, efficiency can

decrease even more in a hyperbaric atmosphere than shown by the estimates of MBC. The fact of the matter is that the maximum effort exerted by respiratory muscles leads to rapid fatigue thereof. The volume of ventilation capable of supporting man for a more or less lengthy period of time does not exceed 50% of the MBC measured in a 15-s test. Even with a maximum muscular load under hyperbaric conditions, pulmonary ventilation does not exceed 86% of MBC [42].

Table 2. Estimated MBC during respiration of normoxic (pO_2 0.21 kgf/cm²) gas mixtures at different pressures

Pressure, kgf/cm²	Diluent gas		
	N_2	He	H_2
1	100*	175	185
5	42	100	122
10	30	77	109
20	22	56	77
30	18	48	67
50	14	37	50
100	10	26	37

*MBC at normal atmospheric pressure in an air environment is taken as 100%.

In this regard, the influence of hyperbaric conditions on overall energy expended by the body is of substantial significance. At low depths, corresponding to a 3-4-fold increase in density of the environment, there is no significant change in human gas exchange at rest or during minimal exercise [46, 54, 55]. With greater increase in density of the environment O_2 uptake and CO_2 output increase [12, 20, 21, 56]. There is a particularly noticeable increase in exchange of gases during intensive exercise performed in a hyperbaric atmosphere [10, 11, 57-61]. Most authors attribute the increase in O_2 uptake in a dense gas environment in part to an increase in function of respiratory muscles; however, the cause of this phenomenon as a whole has not yet been definitively determined.

The increase in expenditure of energy combined with decrease in functional reserves of the respiratory system under hyperbaric conditions may be manifested by inadequate pulmonary ventilation, as compared to the level of metabolic processes in the body. This leads to development of hypoxemic and hypercapnic changes, and respiratory acidosis [7, 11, 12, 26, 28, 40, 45, 47, 56-59, 62, 63]. There are some reports indicative of CO_2 retention by working divers, which resembles the findings in patients with pulmonary emphysema [54, 58, 60, 64-66].

It has been empirically established that the ratio of respiratory function to external work performed by man should not exceed 1.6% and, in the case of prolonged physical exercise, 0.25% [67]. We can make the following estimate on the basis of this rule. Let assume that a diver must perform work of 50 W at a depth of 100 m. This load requires an increase in

pulmonary ventilation to 20-25 ℓ/min. Considering the density of the environment (but not the resistance generated by the breathing equipment), the work of the respiratory muscles will constitute about 0.5 W, i.e., 1% of the useful load. Consequently, man will be able to work for only a short time under such conditions.

On the basis of the results of studies and estimates, some authors concluded that man is capable of performing heavy work (about 200 W) for a short time and moderate work (100 W) for a long time even when there is a 20-fold increase in density of the respiratory environment, as compared to the air at sea level [47]. However, most researchers propose a significantly lower maximum density of the atmosphere: about 9-fold for a moderate load (110-125 W) and 6-fold for submaximum (150-200) brief load [7, 14, 26]. When working in a denser environment, there is development of dyspnea and CO_2 retention in the body [26, 40, 68].

Disturbances in pulmonary exchange of gases under hyperbaric conditions could be attributable not only to the influence of increased resistance to gas flow on the mechanics of the respiratory act. In this case, the changes in alveolar-arterial gradients of respiratory gases (a-Ap_{CO_2} and A-ap_{O_2}), which reflect loss of O_2 and CO_2 tension when passing from the lungs into blood and back, acquire substantial significance. These losses consist of several components, including intraalveolar diffusion of gases, diffusion thereof through the alveolocapillary membrane and presence of an anatomical or physiological arteriovenous shunt. Mathematical analysis of the behavior of each of these components predicts the increase in O_2 and CO_2 gradients in a high density environment [69]. This conforms with Graham's law, according to which the rate of gas diffusion, other conditions being equal, is inversely proportionate to the square root of the density of the gas in question.

However, the results of studies pertaining to A-ap_{O_2} and a-Ap_{CO_2} under hyperbaric conditions are not always by far consistent with such a conclusion. In experiments on anesthetized and artificially ventilated dogs, it was shown that A-ap_{O_2} by no means increases with increase in density of the respiratory environment. In one of these studies [66], breathing gas mixtures varying in density (He-O_2, N_2-O_2, SF_6-O_2) did not affect this gradient, whereas in the case of an SF_6-O_2 mixture combined with pressure elevation to 4 kgf/cm^2 it even decreased. In another study [29], a decrease in a-Ap_{CO_2} was obtained when breathing a dense mixture at normal pressure. The gradient was at a maximum when using an He-O_2 mixture (20.0±3.7), lowest with SF_6-O_2 (14.2±2.6) and between these two when breathing air (16.9±3.2 mm Hg). At the same time, analysis of the results of these studies did not confirm the "increase in efficiency of respiration" in denser gas environments as postulated by the authors: arterial pO_2 when breathing various normoxic mixtures (with He, N_2 and SF_6) was virtually the same (83.7±3.5, 82.8±1.5 and 84.7±2.9 mm Hg, respectively).

Studies of alveoloarterial gradients of respiratory gases in man using respiratory environments varying in density also failed to yield unequivocal results. Thus, virtually the same levels of A-apO_2 were observed with mixtures of He-O_2 and Ar-O_2; however, they were considerably higher than when breathing air [70]. Some increase in A-apO_2 was noted at a pressure of 41 kgf/cm^2 [55]. Some authors believe that this gradient declines due to increase in pO_2 of arterial blood when breathing dense mixtures (Ar-O_2, SF_6-O_2) [19, 44].

In a significant number of the cited works, no consistent influence of density of the gas environment on a-Ap$_{CO_2}$ was demonstrable.

In the opinion of most researchers, the changes in A-ap$_{O_2}$ in a dense environment occur due to change in nonuniformity of layered distribution of gas in the lungs, as well as ventilation-perfusion ratios [19, 22, 23, 25, 69, 71, 72]. For this reason, there is also a change in physiological dead space: it is greater when inhaling denser mixtures (for example, SF_6-O_2) than with less dense mixtures (He-O_2) [7[illegible], 73-75]. Evidently, the influence of density of respiratory mixture, which affects intrapulmonary diffusion, has little effect on the membrane component of the alveolo-arterial gradient. This is indicated by the lack of relationship between diffusion capacity of the lungs and density of the environment; it was demonstrated in several studies, in which this parameter was determined by means of CO (DL_{CO}), that it is about the same when breathing mixtures of O_2 with He, Ar and SF_6 [23, 29]. True, in one such study [75], an increase in DL_{CO} was demonstrated with increase in density of diluent gas, but this finding was attributed in part to the influence of this factor on alveolar ventilation.

As we know, O_2 and CO_2 tension in arterial blood and tissues is the most important criterion of the effect of any factor on transport of respiratory gases in the body. The studies of Chouteau et al. [62, 76] demonstrated that disorders developed in experimental animals (goats), the cause of which the researchers considered to be hypoxemia, with increase in density of the environment by means of raising overall pressure (with retention of normal pO_2) or with a combination of high pressure and the use of an Ar-O_2 mixture. Indeed, elevation of pO_2 in the chamber atmosphere eliminated this phenomenon. Subsequent readings of arterial pO_2 in rabbits confirmed the decrease in blood oxygenation under hyperbaric conditions [77]. It was reported that there was a decrease in amount of oxygen transported by blood per minute in aquanauts, even when they submerged to small depths [78, 79].

In cats exposed to hyperbaric conditions, pO_2 in cerebrocortical tissue decreased while pCO_2 increased with increase in density of the environment (mixtures of He, N and Ar were used) [80]. True, pO_2 of the brain did not drop in dogs inhaling a mixture of He and O_2 at a pressure of 35 kgf/cm^2, whereas in rabbits exposed to an SF_6-O_2 mixture equivalent in density, it even rose somewhat, as compared to the base level [18]. In another study,

where rabbits were exposed to an atmosphere of N_2-O_2 at a pressure of 6 kgf/cm^2, no changes were demonstrated in brain pO_2; however, there was a decrease in oxygenation of arterial blood. But with elevation of pressure to 40 kgf/cm^2, pO_2 of brain tissue dropped [39].

The shortage of information and contradictory nature thereof do not enable us to derive any definite conclusion at this time concerning the effect of the hyperbaric factor on transport of respiratory gases in the body. At any rate, there are no serious grounds to believe that impairment of this transport due to increase in density of the respiratory environment could be the cause of the narcotic effect of neutral gases [45].

Also debatable is the question of whether or not there is a change in intracellular gas exchange in a high pressure atmosphere. There have been reports of decreased O_2 uptake and CO_2 output in some organs of rats exposed to compression of up to 5 kgf/cm^2 [81]. However, other authors do not consider this as any proof of the direct effect of density of the respiratory environment on tissular metabolism [16].

There are several practical considerations that ensue from the facts we have discussed.

It is known that the depths at which a diver or aquanaut can work without being exposed to the adverse effect of hyperbaric conditions can be increased substantially by replacing N_2 in breathing mixtures with He (the density of which is one-seventh that of N_2). While such a replacement at normal atmospheric pressure elicits a beneficial effect on healthy man only in the case of forced breathing [34, 82, 83], at high ambient pressure there is a progressive increase in gain from lowering resistance to respiration by using He-O_2 mixtures [35]. This is confirmed by the data listed in Table 2. At simulated depths of up to 610 m in an atmosphere of He-O_2, alveolar ventilation of the subjects remained normal, both at rest and during minimal exercise [6], whereas in an environment of N_2-O_2 at the same depths (if the narcotic effect could be curbed) man is incapable of physical exertion. Moreover, laboratory mice remained active in an He-O_2 mixture at a pressure of 122 kgf/cm^2, i.e., at a "depth" of more than 1200 m [84].

H_2 could yield an even greater advantage: this gas is half the weight of He (see Tables 1 and 2). According to some data, which are sparse, the H_2-O_2 mixture has a beneficial effect, not only on mechanics of respiration but intrapulmonary exchange of gases [8, 37, 85].

In general, however, as we have seen, no unequivocal results have been obtained as yet concerning the effect of a hyperbaric environment on transport of respiratory gases. The question arises as to whether pO_2 of respiratory mixtures should be raised with increase in depth of submersion. For the time being, there are no grounds for precise recommendations on this

acute. Prolonged exposure to an atmosphere with pO_2 in excess of 0.3-0.5 kgf/cm^2 may cause oxygen poisoning, and this effect is enhanced under hyperbaric conditions [86, 87]. Observations and theoretical estimates suggest that only a slight increase in oxygen content of inhaled mixtures has a beneficial effect, in accordance with the force of the muscular work performed [40, 88-90].

Within the framework of the problems we have discussed, it is deemed important to conduct an in-depth study of the following: range of ambient pressures and time of exposure to such pressures, within which the respiratory system of a working man can cope with the increased load; patterns of effects of hyperbaric conditions on transport of respiratory gases at all stages, including tissues; correlation between changes in respiration and exchange of gases, on the one hand, and other effects of hyperbaric conditions, for example, their effect on nervous system functions, on the other hand; possibility of optimizing the composition of respiratory mixtures intended for use at specific depths with different physical loads (in particular, a physiological evaluation of an N_2-O_2 environment must be made).

Of course, these questions must be answered with due consideration of all factors that affect man when making deep dives.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 612.13-057:629.78

CIRCULATION AT REST IN CREW MEMBERS OF THE FIRST MAIN EXPEDITION ABOARD SALYUT-6

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 11-14

[Article by V. A. Degtyarev, V. G. Doroshev, V. M. Mikhaylov, V. S. Georgiyevskiy, S. A. Kobzev, Z. A. Kirillova, N. A. Lapshina, V. G. Savel'yeva and L. V. Umnova, submitted 13 Feb 79]

[English abstract from source]

The cardiovascular studies did not show any abnormalities in systemic hemodynamics of both crewmembers during their 96-day space flight. At an early stage they exhibited distinct variations of certain cardiovascular parameters which later returned to the normal. These changes are characteristic of individual processes of human adaptation to weightlessness.

[Text] We submit here the results of in-depth medical examinations of crew members who participated in the first main expedition involving a 96-day space flight aboard the Salyut-6 orbital station.

Methods

The crew members were usually examined after their days off. We recorded the tachooscillogram of the brachial artery, sphygmogram of the femoral artery, kinetocardiogram of the left (region of the apex beat) and right (4th intercostal space on the right, near the sternum) heart and pressure in an arm cuff using Polinom-2M equipment, with the subjects at rest. For complex evaluation of circulatory function, we determined the heart rate (HR), minimum, mean dynamic, lateral systolic, end systolic and pulse arterial pressure (AP), duration of phases of isovolumetric contraction (IV) and expulsion of blood (EB) by the ventricles. We calculated the rate of propagation of the pulse wave (RPPW) in the aorta, stroke (SV) and minute (MV) volumes of circulation, specific actual (AR) and functional (FR) vascular resistance.

Hemodynamic parameters of crew at rest aboard the Salyut-6 orbital station

Parameter	Before flight	Flight days										
		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Commander												
HR/min	65 (58—78)	63	67	58	62	68	64	65	72	72	64	67
Minimal AP, mm Hg	71 (66—80)	78	75	68	60	63	67	67	65	61	67	60
Mean dynamic AP, mm Hg	99 (87—120)	113	108	100	84	89	91	108	100	100	105	108
Lateral systolic AP, mm Hg	119 (104—142)	132	130	115	98	108	106	120	110	110	113	117
End systolic AP, mm Hg	142 (120—173)	153	159	153	128	140	137	153	147	146	149	150
Pulse AP, mm Hg	48 (32—70)	54	55	47	38	45	40	53	45	49	46	58
RPPW, m/s	5.8 (4.9—7.0)	9.9	9.1	4.9	8.1	6.0	6.8	7.7	7.0	6.1	5.8	5.6
SV, mℓ	124 (86—171)	69	95	145	69	111	92	107	81	111	113	147
MV, ℓ/min	8.2 (5.7—11.3)	4.5	6.3	8.5	4.3	7.8	5.9	7.0	5.9	8.0	7.3	9.8
SR, arbitrary units	21 (15—28)	46	30	21	34	20	27	27	30	22	25	19
Ratio of SR to proper value, %	117	135	127	117	100	99	108	127	120	118	123	125
Flight engineer												
HR/min	59 (45—65)	60	56	56	59	64	67	67	66	67	64	69
Minimal AP, mm Hg	64 (53—72)	65	54	58	58	62	58	72	66	63	60	58
Mean dynamic AP, mm Hg	87 (73—98)	85	84	78	82	83	78	90	88	82	82	86
Lateral systolic AP, mm Hg	107 (88—120)	109	109	98	90	99	95	105	104	97	97	100
End systolic AP, mm Hg	179 (120—148)	141	140	128	132	138	131	137	142	129	130	118
Pulse AP, mm Hg	41 (39—56)	44	55	40	41	37	37	33	42	34	37	42
RPPW, m/s	6.1 (4.7—7.7)	8.7	8.5	5.8	6.7	6.8	7.0	6.9	5.8	9.7	5.9	6.7
SV, mℓ	177 (77—169)	75	103	119	103	91	95	74	110	50	95	93
MV, ℓ/min	6.9 (4.8—9.1)	4.5	5.8	6.6	6.1	5.8	6.4	4.9	7.3	3.3	6.0	6.6
SR, arbitrary units	25 (19—37)	37	28	23	27	28	24	35	26	48	26	26
Ratio of SR to proper value, %	100	100	100	92	96	96	92	106	109	98	96	100

Note: Range of fluctuations is given in parentheses.

Results and Discussion

There was periodic elevation of AP, associated with increase in SR, during the preflight period in the commander. Pressure was more stable in the flight engineer. Peripheral vascular resistance was consistent with current blood flow rate.

The general condition of crewmen was satisfactory during the mission. In the spacecraft commander, HR was essentially in the preflight range (see Table). His AP was above the mean preflight level on the 7th and 14th flight days due to increased arteriolar tonus. By the end of the first month, it dropped to below base levels. From the 42d day on, there was a tendency toward a second elevation of AP; from the 60th day it became stabilized at the same level, close to the preflight one. Only minimal AP remained somewhat low. As in the preflight period, the cause of AP elevation was constriction of arterioles, as indicated by the fact that actual peripheral resistance was 18-27% above the proper level. There was significant increase in RPPW on the 7th and 14th flight days, with decrease to the lower preflight range by the 24th day; thereafter it usually held at mean preflight levels. SV and MV fluctuated over a wider range in the commander during the 1st flight month than before the flight. Thereafter, the fluctuations decreased, and both parameters remained somewhat lower than the mean preflight levels. By the end of the mission they increased again.

There was virtually no change in HR of the flight engineer up to the 42d flight day, then it began to increase somewhat after the 40th day (see Table). The AP parameters remained within the preflight range throughout the flight. With regard to individual distinctions, it can be noted that minimal, mean and lateral systolic AP remained at the mean preflight levels for the first 2 weeks of the flight, while end systolic pressure rose to maximum preflight levels. Throughout the entire subsequent period, mean and lateral systolic AP were most often below the mean preflight levels, while minimal and end systolic pressure was at the preflight levels. Actual peripheral resistance did not differ appreciably from the proper value. For the first 2 weeks RPPW increased drastically, and thereafter it held at preflight levels. The only exception was the 77th flight day, when the RPPW increased again. SV and MV were essentially in the preflight range, with the exception of the 7th and 77th flight days, when they were lower.

The phase structure of the left ventricle in weightlessness was close to the initial findings in both cosmonauts. However, for the first 2 months there was a distinct tendency toward increased duration of EB. Thus, while it was 0.016 s longer than the proper time for the commander in the preflight tests, it was 0.041 s longer on the 60th day. For the flight engineer, the difference increased from 0.022 s in the preflight tests to 0.038-0.062 s on the 42d-49th flight days. There was some decrease in IC phase of the left ventricle. The demonstrated changes in phases

of the left ventricle leveled off significantly on the 60th-70th days, and the main parameters of cardiodynamics differed little from preflight levels at the final stage of the flight. No appreciable changes were demonstrated in the phase structure of the right ventricle. With regard to individual distinctions, we can mention appearance of negligible deviations in duration of different systolic phases of the right ventricle in the flight engineer on the 7th day. These deviations persisted to the end of the mission, and apparently they were adaptive in nature.

Thus, the results of tests conducted at rest did not, on the whole, demonstrate disturbances of systemic hemodynamics in the course of the 96-day flight. The changes that did occur in some circulatory indices were related to adaptation to weightlessness [1] and development of deconditioning [2], somewhat more marked in the flight engineer. The latter may be related to the fact that he did not perform the recommended amount of physical exercise. Indeed, the changes in intracardiac hemodynamics, which were observed on the 42d-60th flight days, leveled off significantly upon subsequent increase in exercise, which is indicative of their transient nature.

The obtained data characterize the general features of the individual process of adaptation of the human circulatory system to weightlessness, which was manifested by marked fluctuation of some parameters of the cardiovascular system at the first stage of the flight with subsequent relative stabilization at a close to preflight level. In ground-based experiments with simulation of the physiological effects of weightlessness, phasic fluctuations were also demonstrated in some parameters of the circulatory system, which were related to processes of adaptation to new functional conditions [3]. Analysis of the obtained data shows that the adaptation process required about 1-1.5 months of the 96-day flight, after which the parameters of the cardiovascular system became rather resistant to extreme factors. In particular, there was a very typical elevation of AP of the commander at the start of the flight with subsequent normalization. Very similar cardiovascular reactions were observed in the crew of the second expedition aboard the Salyut-4 orbital station, in the course of a 63-day space flight. AP rose during the first month of the flight, then dropped [4].

On the whole, the obtained data are consistent with the results of studies referable to prior long-term space flights aboard the Salyut orbital stations, where no appreciable hemodynamic changes were demonstrated in the crew at rest [5, 6], but there were some signs or other of increased functional strain on the cardiovascular system related to the intensive work of the cosmonauts and development of fatigue. It may be assumed that in-depth examinations on so-called medical days, which usually followed days off, were largely instrumental in minimizing fluctuations of some parameters of the cardiovascular system. A certain amount of preventive measures, with satisfactory work and rest schedule, provided for adequate fitness of the crew and aided in successful completion of the mission as a whole.

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UDC: 612.751.1:612.398]-06:629.78

STATE OF HUMAN PONE TISSUE PROTEIN FRACTION AFTER SPACE FLIGHTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 14-18

[Article by A. A. Prokhonchukov, V. K. Leont'yev, N. A. Zhizhina, R. A. Tigranyan, A. G. Kolesnik and N. A. Komissarova, submitted 18 Apr 78]

[English abstract from source]

Amino acid composition and bone mineralization were studied qualitatively and quantitatively on autopsy of the three crewmembers after their 28-day space flight aboard the orbital station Salyut-1. Sixteen amino acids were detected in the bone protein fraction: cystine and cysteine, lysine, histidine, arginine, aspartic acid, serine, glycine, glutamic acid, threonine, alanine, proline, valine, phenylalanine, leucine and isoleucine, oxyproline. Postflight no abnormalities in the amino acid composition or the bone organic content were found. The role of protein matrices of calcified tissues in mechanisms of bone resistance and adaptation to space flight effects is discussed.

[Text] The question of calcium metabolism during space flights [1-3] is still unclear in many respects, debatable and requires further intensive investigation.

The functional state of protein matrices is the chief factor of dynamic stability (ho ostasis) of bone marrow, its resistance and adaptation to various extreme factors. The protein matrices of bone marrow are "nucleators" [?] of hydroxyapatite crystals, the main crystallite of bone tissue most of which consists of calcium and phosphorus salts. Not only mineralization processes, but remineralization (recrystallization) of bone tissue depend on the functional state of the protein matrices. In the presence of various forms of bone pathology related to loss of calcium salts, recalcification (remineralization) is possible only if the functional properties of the protein matrix are retained. Denaturation of protein structures of the bone matrix and loss of their functional properties make bone recalcification impossible, even if there is adequate saturation of the body with calcium and phosphorus salts, and as a result there may be irreversible changes [4-7]. The fat of lyophilized bone homotransplants is a graphic confirmation of this. They do not "take," and after proliferation by vessels from adjacent tissues they are replaced

by de novo recipient osseous tissue by means of oppositional growth, since the protein matrices of bone tissue are denatured after lyophilization, and they lose their functional properties [4, 6]. Thus, the bone protein matrices are among the main elements in the mechanisms of fixation of calcium and phosphorus.

However, the crystals of osseous hydroxyapatite are not simply oriented on protein matrices, and are connected to them by chemical bonds. Most authors believe that such a bond is formed by phosphoamino acid phosphate: phosphoserine, phosphothreonine phosphohydroxylisine [8, 9], bound with the calcium of hydroxyapatite. There is also a probable phosphoamide bond between the protein matrix and mineral phase [10-12], as well as involvement of phospholipis in protein mineral interactions [5, 13-15]. Changes in protein metabolism developed in the bones of rats after 100 days of experimental hypokinesia, according to the incorporation of ^{14}C-glycine and impaired binding of ^{32}P-phosphate by bone proteins [16, 17].

The objectives of this study included investigation of the state of the protein fraction of human bone tissue after a flight (autopsy findings on the crew of the Salyut-1 orbital station).

Methods

We used samples of bone tissue from the calcaneus. Lipids were removed with a mixture of ethanol and ethyl ether (1:1), then soft tissues were removed; residues of soft tissues and marrow were removed with papain [18]; the samples were then dried to a constant weight, homogenized and decalcified in a solution of 2 N hydrochloric acid and 96° ethanol for 24 h (4°C temperature) with shaking.

The obtained native collagen was dried, then hydrolyzed in sealed vials of 6 N hydrochloric acid at 110°C for 24 h. The hydrolysate was evaporated under vacuum, dissolved in distilled water and submitted to paper chromatography by the method of T. S. Paskhina [19] as modified by V. K. Leont'yev [20]. Amino acids were assayed concurrently by two methods: calibration charts and standard solutions applied on each chromatogram. We took 2-6 concurrent readings for each sample of ossein. We calculated total protein content of bone tissue as the ratio (percentage) of dry collagen weight to the weight of dry unadulaterated bone.

Amino acid composition was determined in molar percentages without consideration of proline content. Hydroxyproline was demonstrated by the method of Neuman and Logan [21] as modified by A. L. Zaydes et al. [22]. No quantitative assay of proline and cystine was made.

Bone tissue from the calcaneus taken from the cadavers of three men who had died of acute trauma at the age of 20-40 years (without pathoanatomically demonstrable signs of visceral or systemic disease) served as a control for comparative analysis.

We calculated the number of required parallel samples and analyses [23, 24] in order to obtain data with a prespecified confidence level (at least 95%). The data were submitted to statistical processing with the use of Student's criterion [23].

Results and Discussion

Organic fraction and total protein content of bone tissue in the group studied did not differ (P>0.05) from control parameters (Tables 1 and 2), and conformed with data in the literature [4, 25, 26].

Table 1. Organic fraction and total protein content of bone tissue (% dry bone weight)

Constituent	Group: under study	control
Organic fraction	36.8±0.9	35.3±0.6
Total protein	28.4±0.7	26.9±0.4

Note: P>0.05 for both parameters.

Analysis of amino acid composition of protein in bone tissue referable to the group under study demonstrated 16 amino acids. Cystine and cysteine (demonstrated together) were present in very small amounts, and they were not assayed thereafter. Lysine and proline were found in all samples; histidine was demonstrated in all samples, but in the form of traces (it was not submitted to quantitative analysis). Threonine was present in small amounts in all samples. Aspartic acid and phenylalanine were present in very small, sometimes trace amounts in all samples.Arginine, glutamic acid, alanine and hydroxyproline were demonstrated in significant and large amounts. Serine, valine, leucine and isoleucine (assayed together) were found in moderate amounts in all specimens. Glycine was present in all samples in the largest amounts (as compared to the other amino acids). A comparison of amino acid composition of bone tissue of the group studied and control group failed to demonstrate qualitative differences. The obtained findings conformed with data in the literature [4, 25, 26].

Quantitative analysis of bone tissue protein in the group under study revealed that it is a type of collagen. Low amounts of cystine, absence of tyrosine, large amounts of aliphatic amino acids, glycine and hydroxyproline were inherent in this protein, as in other collagens. There were relatively minor fluctuations of levels of different amino acids in different samples of the group studied and in parallel readings on the same samples, and they were within the range of the error factor of the reading methods.

Comparative analysis of bones in the group studied and control group failed to demonstrate reliable differences in amino acid composition of total protein (Table 3).

Table 2. Quantitative composition of total bone protein

Amino acid	Main group			Control group		
	1	2	3	1	2	3
Lysine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Arginine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Aspartic acid	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Serine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Glycine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Glutamic acid	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Threonine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Alanine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Valine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Phenylalanine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Leucine + isoleucine	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Hydroxyproline	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Note: Maximum and minimum range of fluctuations is shown in parentheses. The numbers 1 to 3 refer to individual parameters for 3 people in each group.

Table 3. Comparative characteristics of overall amino acid composition of bone protein (in mole %)

Amino acid	Group	
	main	control
Lysine	1.68±0.18	1.46±0.58
Arginine	8.30±0.25	7.41±0.74
Aspartic acid	0.58±0.35	1.27±0.74
Serine	4.73±0.25	4.35±0.70
Glycine	32.46±1.70	32.08±1.29
Glutamic acid	11.60±0.39	12.10±0.32
Threonine	1.54±0.34	1.31±0.18
Alanine	17.60±0.42	18.29±0.64
Valine	2.06±0.37	2.14±0.38
Phenylalanine	0.33±0.16	1.06±0.53
Leucine + isoleucine	3.97±0.47	2.73±0.45
Hydroxyproline	15.91±1.04	15.70±1.13

Note: $P>0.05$ for all parameters.

The obtained data revealed that no deviations whatsoever that could be interpreted as pathological were demonstrable in the state of bone tissue protein fraction after the space flight. This fact has been established

quite clearly on the basis of the results of a complex study of the protein fraction of bone tissue: 1) organic fraction content of bone tissue in the main group did not differ from the control (see Tables 1 and 2); the quantitative and qualitative amino acid composition was identical in the two groups. Data pertaining to amino acid composition of bone tissue protein hold a special place in proof of this thesis. The amino acid composition of total tissular protein is determined by the proportion of individual proteins contained in tissues. The protein of each tissue is characterized by its own unique primary structure and amino acid composition. A change in amino acid composition of total bone protein is a fine indicator of disturbances in tissular protein composition under the influence of various extreme or pathogenic factors. This is particularly important to insoluble tissular proteins, including those of bone, since it is expressly from these indices that one can obtain information about possible changes in these tissues and functional state of protein matrices. This pattern is substantiated by the change in composition of insoluble proteins of decalcified tissues in the presence of various pathological states and diseases.

Thus, on the basis of data in the literature and these studies, it can be concluded that the protein fraction of bone retains its functional properties after a 28-day orbital space flight, including the capacity to fix and retain hydroxyapatite calcium, which was previously demonstrated by direct assay of the mineral fraction, including calcium and phosphorus of skeletal bones [2]. The findings obtained in this study lead us to expound the following hypothesis. Since protein matrices of bone retain their functional properties of fixing calcium and implementing remineralization processes under space flight conditions, it is obvious that various methods and means of stimulating remineralization of bone tissue during space flights are implemented expressly by retention of these properties as determining the main mechanism of remineralization (recrystallization) of bone, which is the basis of its resistance and adaptation to the extreme factors of space flights. This thesis is confirmed by data to the effect that the efficacy of thyrocalcitonin in normalizing bone tissue function is significantly enhanced when it is combined with retabolil [deca-durabolin], which has a selective action expressly on the protein fraction of bone tissue [27].

On the basis of our analysis of the literature and results of the studies, we can expound the assumption (in the nature of a working hypothesis) that the normal state of the bone protein fraction after the space flight could be attributable to the high level of physical training and conditioning of the cosmonauts, with subsequent use aboard the orbital station of the set of equipment and conditioning measures directed toward precluding the undesirable effects of flight factors on man [2, 28, 29].

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UDC: 59.082:629.78

RESEARCH HARDWARE AND HABITAT OF ANIMALS USED IN EXPERIMENT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 18-22

[Article by B. A. Adamovich, Ye. A. Il'in, A. D. Noskin, V. I. Milyavskiy, G. N. Pliskovskaya, V. K. Golov, V. S. Poleshchuk, V. K. Ovcharov and A. A. Shipov, submitted 7 Aug 79]

[English abstract from source]

The paper reviews the hardware used to provide life support to experimental animals (rats) and to obtain information inflight. The hardware includes two specially designed centrifuges to generate artificial gravity. The paper describes the environmental parameters in the mock-up cabin and field laboratories used at the recovery site

[Text] The next specialized biological satellite, Cosmos-936, was launched in the USSR on 3 August 1977. The research program scheduled for this biosatellite included a continuation of the study of the effects of space flight factors on various biological objects, as well as investigation of the possibility of using artificial gravity [AG] as a means of preventing the adverse effects of weightlessness. The objectives and conditions for the physiological experiments with animals (rats) were described in detail previously [1].

An automated complex of scientific hardware was developed and constructed for the studies aboard Cosmos-936, as was done for the experiments conducted on other biosatellites [2-5]. This complex provided for optimum maintenance conditions for the animals, bioengineering monitoring of their condition, delivering oxygen to animals, removing toxic gas impurities from the pressurized cabin of the biosatellite, maintaining comfortable temperature and humidity levels in the cabin.

The research program for the Cosmos-936 biosatellite differed from others in that mammals were exposed to AG of 1 G, and this was the first time this was done in space. For this purpose, two centrifuges were installed

aboard the satellite, each holding five animals (Figure 1). The velocity of rotation of the centrifuges during the flight constituted 53.5±3 r/min, and AG constituted 1 G over a radius of 320 mm (up to the arbitrary longitudinal axis of the animal). Another group of animals was kept in cages that were a part of the automated units analogous to those used in previous flights.

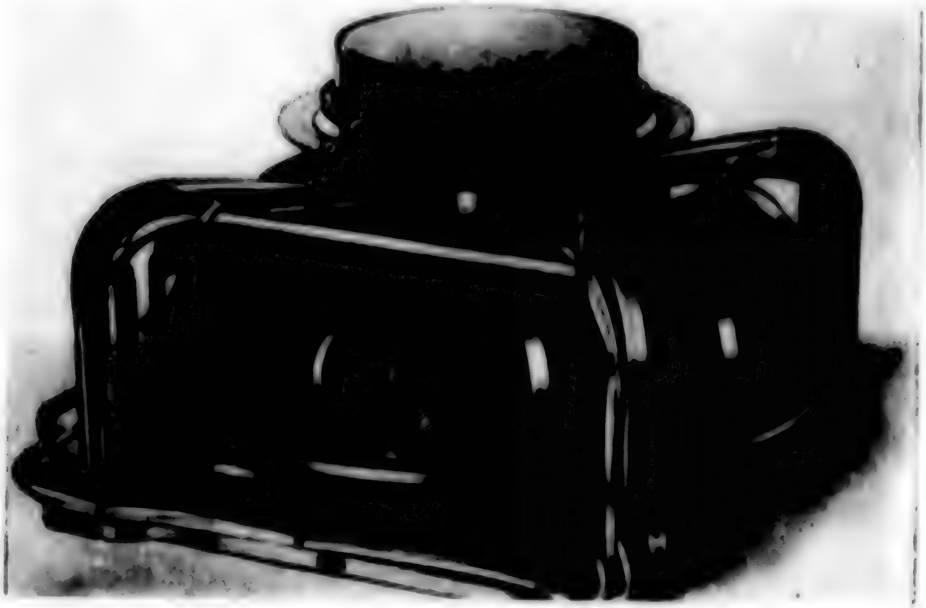

Figure 1. Onboard centrifuge to expose rats to AG

The life support conditions, as well as interior of the cages, both on the centrifuge and in the stationary units were analogous, in spite of their apparent difference externally. There were a feeder, water dish, light fixture, system of ventilation holes, slitted device with a screen to remove excrements and a container for them within the cage. Each cage was equipped with a measuring device that added up the movements made by the rats. Sensors were implanted in some of the animals to measure body temperature.

Essentially the same automated systems for regeneration of the atmosphere were used here as in the experiments on previous biosatellites in order to maintain comfortable temperature and humidity levels in the pressurized

cabin, to deliver oxygen to the animals, remove carbon dioxide and toxic gas impurities from the air environment.

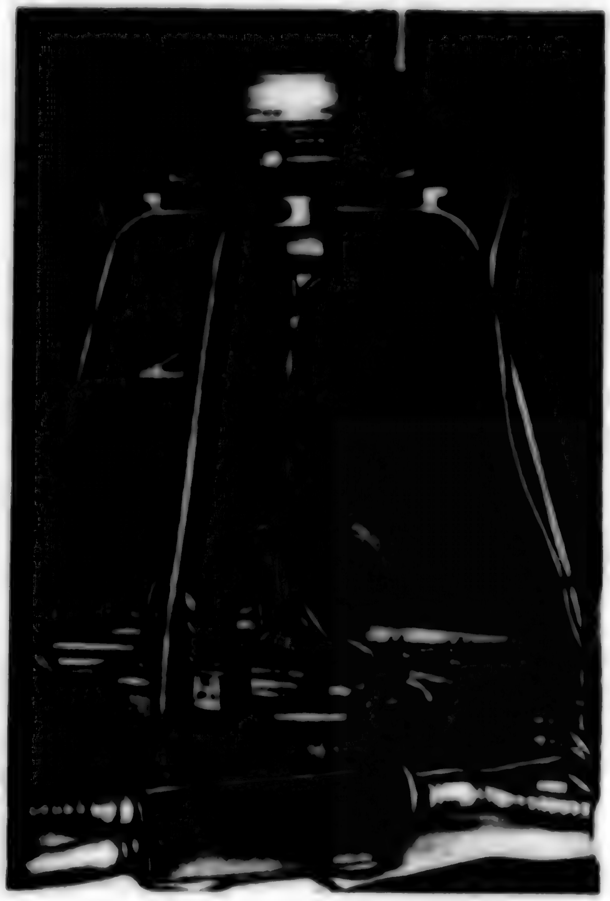

Figure 2. Ground-based short-arm centrifuge for control experiment

During the flight, oxygen content of the descent vehicle constituted 145-210 mm Hg and carbon dioxide did not exceed 14 mm Hg; relative humidity was held at 80-90%.

Much attention was devoted to the quality of the air environment in the cabin, one of the important parameters of which was the amount of toxic gaseous compounds in this environment. The sources of such compounds aboard biosatellites are various polymers, the animals themselves and

particularly their liquid and solid excrements. As shown by the results of special studies, there was consistent presence of gas impurities, the main component of which was ammonia, in the air environment of mockups of Cosmos-605, Cosmos-690 and Cosmos-782.

An autonomous system was installed aboard Cosmos-936 to remove gase impurities from the air environment. This system was turned on by command from the ground on the 10th day of the flight, and it was in operation until the mission was completed.

The results of studies of levels of the main gas impurities in the air environment of the mockup of Cosmos-936 revealed that there were trace concentrations of acetone, aldehydes and organic acids. Ammonia and other amino compounds were an exception, and their level reached 8.0 mg/m^3 at the end of the experiment. The concentration of organic compounds was in the range of 48-144 mgO_2/m^3. These findings indicate that the use of a refined system for cleaning the atmosphere aboard Cosmos-936 improved significantly the hygienic conditions of the air environment in the habitat of the experimental animals.

The life support system for the animals, gas analyzers for oxygen, carbon dioxide and water vapor, as well as thermostats and other instruments aboard Cosmos-936 made up a single automated complex. A complex control unit was used to issue and place commands, switch over the electric circuits used for different purposes, communicate with the radiotelemetry and power systems of the satellite.

The ground-based, synchronous control experiment was an important element of the studies aboard Cosmos-936. For this purpose, the same habitat was reproduced in the mockup on the basis of telemetry data delivered from the biosatellite as in the pressurized cabin of the latter during the flight, with the exception of weightlessness and ionizing radiation. The data concerning parameters of the air environment were reproduced in the ground-based experiment with the following error factor: ±2% for oxygen, ±2% for carbon dioxide, ±1% for air temperature and 5-10% for relative humidity. The use of an automatic system of regulating and holding the microclimate parameters aided in such close reproduction of the air environment in the synchronous experiment. This system made it possible not only to maintain rather accurately the microclimate parameters within the required range, but to regulate on an ongoing basis the temperature, humidity and pressure in the sealed space of the mockup of the biosatellite.

Rotation of a group of animals on a short-arm (92 mm) centrifuge (Figure 2) at a rate equal to the rate of the onboard centrifuge was an element of the program for the ground-based control experiments. Two such centrifuges were used, with five animals on each. The purpose of the experiment was to determine the role of the rotation factor in the changes in physiological parameters of animals aboard the biosatellite and exposed to a 1-G artificial gravity.

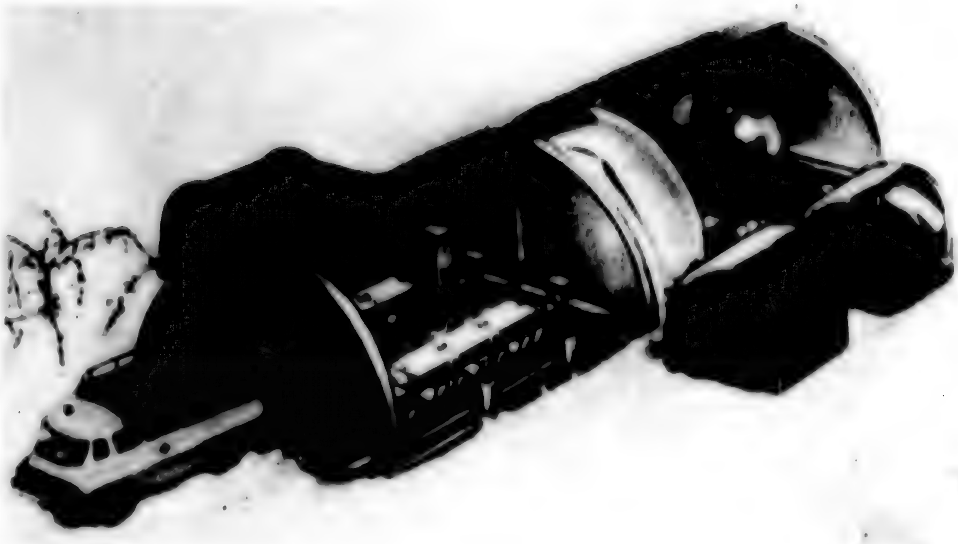

Figure 3. General view of search and rescue complex for conducting scientific research work at the biosatellite landing site

A search and rescue complex, based on a field laboratory, which consisted of a system of inflatable tents with hardware and equipment in them, was developed and constructed for conducting studies at the landing site of the descent vehicle (Figure 3). A total of 50 people could work at the same time in such a laboratory. It was equipped with a miniature power station, air conditioning and microclimate maintaining systems.

The descent vehicle of the biosatellite landed at 0627 hours on 22 August 1977. After 45 min, the descent vehicle was placed in one of the sections of the field laboratory; then the modules were opened, disassembly work was done and the animals were removed. The animals were examined 3.5 h after the descent vehicle landed.

The results of the scientific studies conducted during the experiment aboard Cosmos-936 warrant the belief that the principles serving as the basis for building the life support systems and scientific hardware are valid and have justified themselves entirely.

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UDC: 612-019:599]:629.78

PRINCIPAL RESULTS OF PHYSIOLOGICAL EXPERIMENTS WITH MAMMALS ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 22-25

[Article by O. G. Gazenko, Ye. A. Il'in, A. M. Genin, A. R. Kotovskaya, V. I. Korol'kov, R. A. Tigranyan and V. V. Portugalov, submitted 12 Apr 79]

[English abstract from source]

The program of the 18.5-day flight of the biosatellite Cosmos-936 included studies of physiological effects of prolonged weightlessness (20 rats) and artificial gravity (10 rats). The latter produced a normalizing effect on the function of the myocardium, musculo-skeletal system and excretory system. Simultaneously, artificial gravity exerted an adverse effect on the functions dependent on several sensors, primarily optic, vestibular and motor sensors. It is postulated that the adverse effects are associated with a relatively high rate of rotation and a short arm of the centrifuge.

[Text] The solution of the problem of creating artificial gravity [AG] amounts ultimately to experimental substantiation of the minimal level of gravity at which the adverse effects of weightlessness were eliminated and customary living conditions were provided for the crew.

The AG parameters for manned flights should be determined through direct tests on man. At the same time, experiments with animals make it possible to provide comprehensive substantiation for the use of AG as a means of preventing the adverse effects of weightlessness and, moreover, to assess the negative effects of rotation factors associated with generation of AG.

For the first time in cosmonautic practice, experiments aboard Cosmos-782 biosatellite with plants and lower vertebrates established that the biological effect of AG is basically the same in nature as the effect of earth's gravity. The experiment aboard Cosmos-936, the main objectives and conditions of which were described previously [1], was a logical continuation of the studies pursued aboard the Cosmos-782 biosatellite (1975).

During the orbital flight aboard Cosmos-936, the condition of the animals, as determined according to their overall motor activity and body temperature, was quite satisfactory. The level of overall motor activity was subst tially higher, while mean daily body temperature was lower in animals exposed to weightlessness than animals exposed to AG of 1 G (V. S. Oganov, V. Ya. Klimovitskiy).

The long-term flight aboard the biosatellite affected the general condition and postural-motor reactions of the animals in the postflight period. The greatest changes were found in rats exposed to weightlessness. They were sluggish, spent most of the time stretched out; they moved by crawling, or else with drastically altered gait. There were none of the typical movements and positions related to the orienting reaction in a new situation. Less marked changes were noted in animals exposed to AG. They were more active, overcame obstacles well, got up on their hind legs, and their gait was close to normal.

Static endurance, which was diminished after the flight in all cases, was restored sooner in rats exposed to AG, and it also reached the proper level sooner by the 6th day of the postflight period.

There were no appreciable differences in weight gain by experimental groups of animals. However, the rate of weight gain was higher in animals exposed to AG than those in the weightlessness group.

Moderate signs of a stress reaction were noted in animals submitted to weightlessness: increased functional activity of the adrenal cortex, hypoplasia of the thymus and spleen, increased percentage of segmented nuclear neutrophils in peripheral blood, lymphopenia and eosinopenia. Such changes were either absent or extremely insignificant (peripheral blood) in animals exposed to AG.

Microbiological and immunological studies revealed proteus in the throat and decline of class G immunoglobin level in blood serum of animals submitted to weightlessness, unlike those exposed to AG; this was indicative of some weakening of protective properties of their organism.

On the 3d day of the readaptation period, there was a statistically significant decrease in exchange of gases in animals submitted to weightlessness, unlike those exposed to AG during the flight.

The test with a water load (5 mℓ/100 g weight), conducted on the 1st day of the readaptation period to assess the osmoregulatory system and possible liquid shortage in the body, failed to demonstrate any differences in dynamics and maximum levels of diuresis between the two experimental groups of rats. At the same time, there was reliable greater excretion of sodium in urine after the water load test in animals exposed to weightlessness than in rats exposed to AG and in the ground-based control experiments.

Administration of a potassium load (1.25% KCl) on the 2d day of the re-adaptation period led to virtually the same excretion of fluid in animals from different experimental groups. However, there was greater excretion of potassium (349±24.6 meq/100 g) in animals exposed to weightlessness than in rats submitted to AG (262±43.9 meq/100 g) and animals in the ground-based synchronous experiment (228±2.7 meq/100 g). Thus, the greatest changes in ion regulating function of the kidneys were demonstrated in rats submitted to weightlessness during the flight. AG had a normalizing effect on renal excretion of sodium and potassium.

The absence of any disturbances referable to the structure of individual nephrons of rats in all experimental groups warrants the belief that the changes in electrolyte metabolism (at least the increased excretion of potassium by animals exposed to weightlessness) is the result of a change in basal metabolism and, first of all, metabolism of the muscular system (Yu. V. Natochin).

Exposure to weightlessness led to appearance of distinct signs of atrophy and metabolic disturbances (change in spectrum of lactate dehydrogenase isozymes, accumulation of glycogen, increased phospholipid content and ALT activity) in the muscles of the limbs, particularly the soleus. We observed development of moderate atrophic changes in the same muscles of rats exposed to AG during the flight; however, they usually failed to present metabolic changes.

Both experimental groups of animals presented significant worsening of blood supply to muscles, as indicated by the decreased number of functional capillaries.

Weightlessness led to an increase in amount of sarcoplasmic proteins and significant decrease in ATPase activity of myocardial myosin. No changes were observed in amount of myocardial sarcoplasmic proteins in animals exposed to AG, while the decrease in myosin ATPase was less marked.

Examination of the femoral and tibial bones of rats submitted to weightlessness revealed slower growth rate, development of osteoporosis, decreased density and mineralization, as well as 30% decrease in mechanical bending strength. Use of AG prevented changes in calcium and phosphorus content of long bones.

Studies of the function of the vestibular analyzer revealed that prolonged weightlessness did not alter the function of the semicircular canals (A. A. Shipov), while sensibility of the otolithic system diminished (G. S. Ayzikov). Long-term exposure to a system with AG, on the contrary, failed to alter otolith function; however, it diminished sensibility and reactivity of the semicircular canals. Consequently, in both instances, absence of change in function of one part of the vestibular system is associated with a change in function of the other. This could cause an intra-labyrinthine conflict concerning information about a movement. The

existence of such a conflict is probably one of the causes of a poor turning reflex and poorer equilibrium function in animals exposed to both weightlessness and AG.

Morphological studies revealed only insignificant ultrastructural changes in the vestibular system, which were equally marked in animals exposed to weightlessness and AG (Ya. Vinnikov).

Examination of higher nervous activity (capacity for orientation in a maze) revealed that the functional changes were more significant in animals kept on the centrifuge during the flight than in those submitted to weightlessness. There was particularly graphic manifestation of this when the tests presented to the rats were more complicated (N. N. Livshits).

Biochemical studies of brain structures responsible for higher motor control revealed that there was the most significant decline in RNA content of Purkinje cells of the cerebellum and decrease in H group content of the tissue of the frontal (motor) cortex of animals exposed to AG during the flight.

Thus, studies of the main physiological systems of rats that were weightless for 18.5 days revealed changes analogous to those demonstrated in previously conducted experiments aboard biosatellites of the Cosmos series [2-4]. These changes can be arbitrarily divided into nonspecific (development of fatigue, decreased nonspecific resistance, appearance of signs of a stress reaction) and specific (change in vestibular function, muscular atrophy, osteoporosis of long bones, changes in the myocardium and excretory system). In most cases, the nonspecific and specific reactions to weightlessness were usually no longer demonstrable by the 25th day of the readaptation period.

Creation of AG of 1 G during the space flight prevented to a significant extent development of the above-mentioned adverse changes in the animals. Special mention should be made of the normalizing effect of AG on the functional state of the myocardium, skeletomuscular system and excretory system. Along with the beneficial effect of AG on the animals, we found some adverse effects on functions, the performance of which is implemented by the concurrent activity of several analyzers, first of all the visual, vestibular and motor (function of equilibrium, turning and landing reflex, orientation in the maze and higher motor control).

The demonstrated differences in the tested parameters of animals exposed to AG and natural gravity are probably attributable to the relatively high rate of rotation of the centrifuge (53.3 r/min) and its short arm (320 mm).

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UDC: 612.856.3-06:629.78

SEMICIRCULAR CANAL FUNCTION IN RATS AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 25-30

[Article by A. A. Shipov and V. G. Ovechkin, submitted 26 Dec 78]

[English abstract from source]

The nystagmus reflex latent period, total and mean number of events and their duration were measured in the rats flown for 18.5 days aboard the biosatellite Cosmos-936 under the conditions of weightlessness and artificial gravity. The studies demonstrated that prolonged weightlessness did not influence the receptor formations and centers of semicircular canals. A long exposure to artificial gravity brought about a decrease in reactivity and sensitivity of semicircular canals. The mechanisms of these phenomena are discussed.

[Text] Substantial disturbances referable to postural and certain motor reactions were demonstrated in rats after an 18.5-day flight aboard the Cosmos-782 biosatellite. Generally, the findings were indicative of temporary functional insufficiency of the motor and vestibular analyzers [1]. For this reason, much attention was devoted to the study of vestibular function in the experiment aboard Cosmos-936. It was of special interest to study the group of animals exposed to artificial gravity [AG]. The fact of the matter is that vital functions of animals in a rotating system are related to prolonged exposure of the body and, in particular, the vestibular system, to Coriolis and precessional accelerations [2]. Such factors can lead to a change in vestibular function, locomotion, opticomotor coordination and, ultimately, to impairment of equilibrium.

In this work we submit the results of a comparative study of the functional system [3] of the semicircular canals of rats after flying aboard Cosmos-936 in weightlessness and under AG of 1 G.

Methods

Experiments were conducted on 25 male SPF Wistar rats with an initial weight of 210-230 g. The animals were divided into 5 equal groups: FW,

and FC_3--animals flowing in space for 18.5 days and exposed to weightlessness and AG, respectively; SW_3--rats used in a ground-based synchronous experiment, in which the habitat aboard the biosatellite and dynamic factors inherent in the launching, descent from orbit and landing phases were simulated; C_3--animals rotated in a short-arm ground-based centrifuge at the rate of 53.3±0.3 r/min, with the same angular velocity of rotation of the onboard centrifuge and, finally, VC_3--animals in the vivarium control. The existence of three ground-based control groups made it possible to differentiate between the influence of the factors of weightlessness, rotation (precessional and Coriolis accelerations), upkeep conditions, as well as repeated tests for changes in the reactions studied. The experimental conditions aboard Cosmos-936 were described in detail previously [4].

We assessed the function of the semicircular canals according to changes in characteristics of the nystagmic reflex in response to a series of increasing angular accelerations (10, 20, 30, 40°/s^2). The animals were rotated on a trapezoidal program: positive acceleration for 3 s, rotation at a constant rate for 1 min, negative acceleration. With each acceleration they were rotated once, and the direction of rotation for each subsequent acceleration was the opposite of the preceding one [5].

Nystagmus was assessed on the basis of the latency period (measured from the start of rotation to the start of the rapid phase of the first nystagmic jerk), number of jerks, duration and mean frequency of jerks (quotient from dividing the number of jerks by duration of nystagmus).

The animals were examined 2 weeks before the flight and start of ground-based control experiments, as well as on the 2d, 7th, 12th, 15th and 23d days of the readaptation period. The landing day was considered as 0 day of the readaptation period.

The obtained data were submitted to statistical processing, with the use of Student's criterion ($P<0.05$).

Results and Discussion

Background tests revealed that the correlation between the nystagmus parameters studied and magnitude of acceleration did not differ basically from the one previously described [6-10].

In the VC_3 group of animals, successive testing of the latency period of nystagmus did not differ from the background findings. The number of jerks, duration and frequency of nystagmic jerks decreased from test to test. The decline of nystagmus parameters was indicative of habituation to angular accelerations at the subsequent examinations [9-10].

At all tested times and with all levels of accelerations used, we failed to demonstrate reliable differences between the FW_3, SW_3 and VC_3 groups with regard to such parameters as latency period, number of jerks (with the

exception of acceleration of 40°/s on the 2d day), duration (Figure 1) and frequency of nystagmic jerks. Thus, long-term weightlessness did not cause an appreciable change in sensibility and reactivity of the functional system of the semicircular canals or nature of habituation to repeated exposure to angular accelerations.

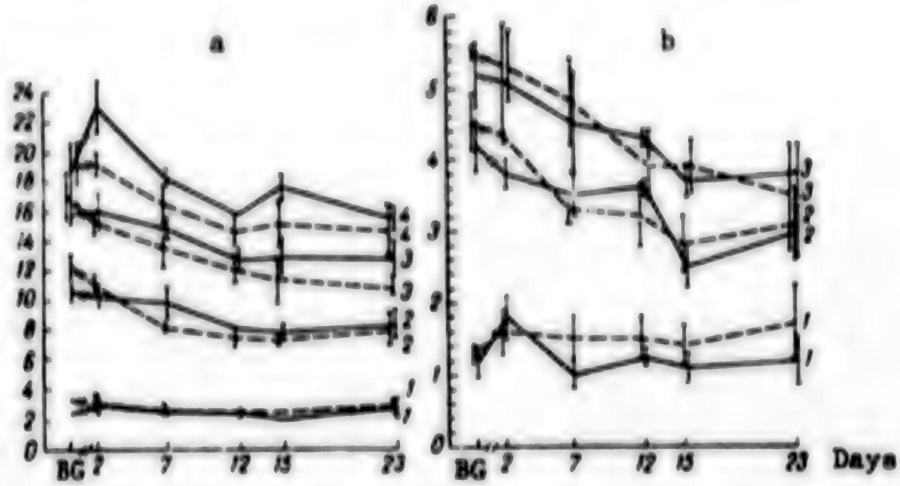

Figure 1. Number of nystagmic jerks (a) and duration of nystagmus (b, in seconds) during rat readaptation following 18.5-day flight aboard Cosmos-936 in weightlessness. The solid line refers to the FW_1 group and the dash line to SW_1. X-axis, day of examination. 0 day refers to day of end of experiment. 1-4--accelerations of 10, 20, 30 and 40°/s², respectively. BG--background.

Very different patterns of changes in the parameters tested were found in animals rotated on the centrifuge upon analysis of their nystagmic reaction. On the 2d postflight day, a distinct tendency toward longer latency period of the nystagmic reaction to accelerations of all tested levels was observed in the FC_2 group of animals (Figure 2). The C_2^0 group also presented an increase in latency period, which was reliable with accelerations of 10, 20 and 30°/s². On the 7th day, the duration of the latency period of nystagmus did not differ from the background levels with accelerations of 20, 30 and 40°/s². With 10°/s², restoration of the latency period took a longer time (see Figure 2). We failed to demonstrate reliable differences between animals in groups FC_2 and C_2^0, with regard to latency period of the nystagmic reaction. Thus, when animals were kept in a rotating system for a long time there was temporary increase in latency period of the nystagmic reaction, i.e., decreased sensitivity of functional systems of the semicircular canals to angular accelerations. It should be noted that Clark [11], who studied the latency period of nystagmus in rats following prolonged (up to 60 days) rotation on a ground-based centrifuge (41 cm radius, 62 r/min, 2 G),

also observed a reliable increase. Comparable results were also obtained from analysis of the thresholds of the nystagmic reaction of rabbits after 15 days of rotation on a centrifuge (100 cm arm, 3 r/min) [6]. The increase in latency period of the electromyographic reaction of muscles of rat hind legs to rotation of the animals about the longitudinal body axis [12], increase in spontaneous motor activity of rats upon repeated placement in a revolving system [13], as well as data [14] pertaining to a decrease in threshold sensitivity of chickens to angular accelerations after prolonged rotation (180 cm arm, 25 r/min, 1.5 G for 35 days and 30 r/min, 2 G for 49 days) are also indicative of decreased sensitivity to vestibular stimuli after being kept in rotating systems. Our studies supplement the findings of the above authors in that they demonstrate the brief nature of increased thresholds of sensitivity of the semicircular canals according to indices of somatic reactions to angular accelerations. In our opinion, the longer time required for restoration of the latency period of nystagmus with the lowest of the tested accelerations ($10°/s^2$) is attributable to the fact that this parameter is particularly sensitive to the state of the central nervous system [8, 15], which changes appreciably after rotation [16], in the case of using low accelerations.

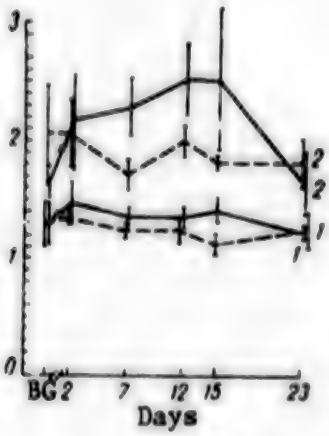

Figure 2.
Latency period of nystagmus (s) in rats after 18.5-day flight aboard Cosmos-936 with AG; Solid line, FC_2 group; dash line FW_3; 1 and 2—20 and $10°/s^2$ accelerations, respectively; BG—background.

Examination on the 2d day of the aftereffect period revealed a reliable decrease in number of nystagmic jerks in animals of groups FC_2 and C_2^0, as compared to both background levels and data for animals in groups FW_3, SW_3 and VC_3. Figure 3a illustrates this on the example of change in nystagmic reaction to $30°/s^2$ acceleration. There was a high level of significance of differences with accelerations of 40, 30 and $20°/s^2$ ($P<0.001$). The routine examination on the 7th day of the readaptation period revealed that the number of nystagmic jerks not only failed to decrease, as compared to the 2d day, it even increased, and the higher the acceleration level, the more it increased. In group C_2^0 animals, this increase was reliable with all tested levels of accelerations, and in group FC_2, it was reliable with accelerations of $20°/s^2$. Thereafter, there was slower increase in number of jerks, and this was followed by a tendency toward decrease (Figure 3a). However, even on the 23d day, the number of nystagmic jerks was greater than on the 2d day. Analogous patterns were inherent in the curves of duration of

nystagmus (Figure 3b). The curves of dynamics of frequency of nystagmic jerks show only a tendency toward such changes. The parameters of nystagmus were the same in all groups of animals on the 7th-12th days. At all times tested, we failed to demonstrate differences in reactions to acceleration and deceleration of rotation according to all of the tested parameters of nystagmus.

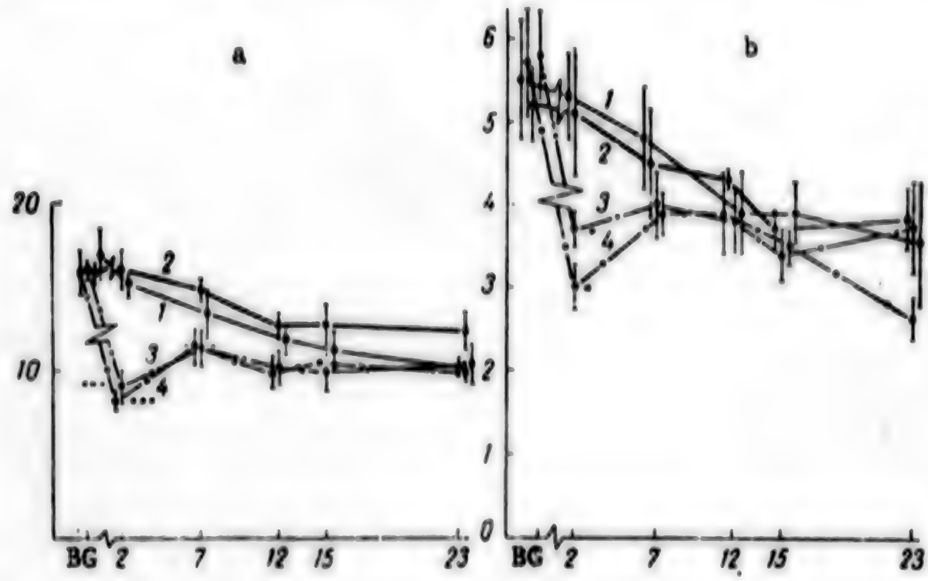

Figure 3. Number of jerks (a) and duration of nystagmus (b; in s) in rats during readaptation period after 18.5-day flight aboard Cosmos-936 with AG. In all cases angular acceleration constituted $30°/s^2$.

BG) background
1-4) SW_3, FW_3, FC_2 and C_2^0 groups, respectively
*) $P<0.05$, as compared to indices for group SW
***) $P<0.001$

A decrease in some parameters of the nystagmic reaction was observed in man during prolonged presence in a rotating system [17, 18]. In experiments conducted on chickens, it was found that there was significant decrease in the nystagmic reaction when first tested on the day of termination of prolonged rotation; it increased thereafter, which is indicative of disappearance of habituation to repeated exposure to angular accelerations [14]. It was also noted that the higher the level of gravity at which prolonged rotation occurred, the more significant the initial decrease in the reaction and the fuller its restoration at subsequent tests. In our study, we observed a similar change in nystagmic reaction of animals in groups FC_2 and C_2^0, but it was less marked (see Figure 3).

In our opinion, the unique dynamics of parameters of the nystagmic reaction, as demonstrated in the successive tests during the aftereffect period following prolonged rotation, are indicative of onset of complex residual [trace] processes in the nystagmogenic centers. These processes are induced by prolonged and combined stimulation of receptors of the semicircular canals by precessional accelerations and receptors of the otolith system by Coriolis accelerations, which arise with spontaneous head movements in the rotating system. Indeed, with concurrent stimulation of both parts of the vestibular system during eccentric rotation, subsequent stimulation only of receptors of the semicircular canals induces changes in parameters of nystagmus [19] similar to those we demonstrated.

Thus, analysis of the changes in nystagmic reaction of rats (according to such parameters as latency period, number of jerks, duration and mean frequency of jerks) in response to a series of accelerations increasing in level failed to demonstrate appreciable changes, i.e., the sensitivity and reactivity of the functional system of the semicircular canals did not change in animals after exposure to weightlessness. This may indicate that prolonged weightlessness does not affect receptor elements and centers of the semicircular canals. Perhaps, these influences are so insignificant and brief that they cannot be demonstrated on the 2d day after landing.

Prolonged stays of animals in a system with AG leads to a decrease in reactivity and temporary decrease in sensitivity of the functional system of the semicircular canals during the aftereffect period, as a result of prolonged and concurrent stimulation of the semicircular canals by precessional accelerations and receptors of the otolith system by Coriolis accelerations. The temporary decrease in sensitivity of the functional system of the semicircular canals could lead to a need for use of considerably higher angular accelerations for an animal placed in a situation that makes it difficult to retain equilibrium (mobile or unstable support, narrow bar) in order to alter muscle tone of antigravity muscles when equilibrium is impaired. Under such conditions, we could expect an increase in amplitude of angular movements of the head and body, and rapid loss of equilibrium due to the impossibility of fine control of postural tonus by the vestibular analyzer [11].

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UDC: 616.42-007.23-092.9-02:629.78

ROLE OF DYNAMIC SPACE FLIGHT FACTORS IN THE PATHOGENESIS OF INVOLUTION OF LYMPHATIC ORGANS (EXPERIMENTAL MORPHOLOGICAL STUDY)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 30-35

[Article by A. S. Kaplanskiy and G. N. Durnova, submitted 5 Sep 78]

[English abstract from source]

The role of the dynamic factors in accidental involution of lymph organs has been investigated in a ground-based study simulating a 20-day space flight. It has been inferred from the study that lymph organ involution observed in rats exposed to prolonged space flights is caused by chronic and acute stresses. Chronic stress is associated with weightlessness and leads to hypoplasia of lymph organs; acute stress is connected with the transition from weightlessness to normal gravity (gravity stress), thus enhancing chronic stress induced lymph tissue hypoplasia. Spleens of both weightless and hypokinetic rats show inhibition of erythropoiesis and accumulation of hemosiderine due to accelerated erythrocyte degradation caused by diminished motor activity.

[Text] In previous studies [1-3], it was often observed that there is accidental involution of lymphatic organs of rats that spent a long time aboard a biosatellite. Development of hypoplasia of lymphatic tissue of animals was interpreted as a result of the stressor effect of the extreme factors of the space flight. However, the significance of each of them to the pathogenesis of lymphatic hypoplasia remained unclear, since the changes demonstrated in lymphatic organs of rats after landing of biosatellites constituted the overall effect of several such factors, which were active at different phases of the space flight.

In this study, we have tried to determine the role of weightlessness and other extreme space flight factors in development of lymphatic hypoplasia, and we used for this purpose the results obtained from a ground-based model experiment.

Methods

Experiments were conducted on 74 male Wistar rats from an SPF colony, with initial weight of about 240 g. We simulated stressor factors, which occur

during launching and landing of biosatellites, as well as gravitational stress, which develops when changing from weightlessness to earth's gravity, by means of 5-h immobilization on special stands, with the animals in prone position, using a method developed at the Institute of Experimental Endocrinology of the Slovak Academy of Sciences [4, 5]. To simulate weightlessness in the ground-based experiment, we put the animals in small box-cages, which restricted movement, for 20 days (the time corresponding to mean duration of biosatellite flights). The data of a number of authors, indicating that hypokinesia under ground-based conditions reproduces rather well the main biological effects of weightlessness [6-8] served as grounds for using hypokinesia as a model of weightlessness.

All of the animals were divided into 7 groups: the 1st, 2d and 4th groups consisted of 5, 9 and 5 rats, respectively, which were sacrificed immediately, 5 h and 20 days after 5-h immobilization; the 3d group consisted of 10 animals sacrificed immediately after 10-h immobilization; the 5th consisted of 5 rats submitted to hypokinesia for 20 days after 5-h immobilization; the 6th consisted of 9 rats submitted to 5-h immobilization twice (20-day interval); the 7th consisted of 10 animals that were immobilized for 5 h, kept under hypokinetic conditions for 20 days and then submitted again to 5-h immobilization. We used 25 intact rats as a control; they were kept in the vivarium and sacrificed at the same times as experimental animals. We weighed the thymus and spleen of experimental and control rats, then fixed them in Carnoy fluid and imbedded them in paraffin. Organ sections were stained with hematoxylin-eosin, methyl green-pyronine and picrofuchsin. We measured the area of white pulp of the spleen using enlarged photographic prints of spleen cross sections. [9].

Results and Discussion

According to the data listed in the Table, there was no decrease in weight of the thymus and spleen of rats in the 1st group, whereas animals in the 2d and 3d groups presented a decrease in spleen weight with no change in the thymus. In the 4th group of rats, the weight of the thymus and spleen did not differ from that of control animals. At the same time, there was a decrease in thymus weight of rats in the 5th group, and there was a distinct tendency toward decrease in spleen weight. The second 5-h immobilization 20 days after the first immobilization for the same time (6th group) led to a decrease in spleen weight, with no change in the thymus. Finally, in the case of repeated immobilization of the rats following the first 5-h immobilization and 20 days of hypokinesia (7th group), there was a decrease in weight of the thymus and spleen.

Histological examination of the thymus of rats in the 1st, 2d and 3d groups revealed massive accumulation of nuclear detritus, due to massive breakdown of lymphocytes, in the cortical substance of all animals. In the rats of the 2d and 3d groups, there was the same amount of nuclear detritus, which was considerably greater than in the thymus of the 1st group of rats.

Along with nuclear detritus in the cortical substance of the thymus in rats of the 2d and 3d groups, we encountered numerous macrophages that phagocytized the nuclear detritus(there was no macrophage-phagocytic reaction in the thymic cortex of rats in the 1st group). In all three of the groups mentioned, there was some vagueness of the boundary between the cortical and medullary substance.

Thymus and spleen weight, area of white pulp of spleen in experimental and control rats (M±m)

Group	Nature of experiment	Wt. of thymus mg	P	Wt. of spleen mg	P	White pulp area in arbitrary units	P
1	Immobilization, 5 h (n=5)	606±26	<0.4	555±53	<0.2	502±62	<0.5
	Vivarium control (n=5)	650±39		670±56		483±39	
2	Immobilization, 5 h, + 5-h rest (n=9)	444±39	<0.4	415±14	<0.001	262±13	<0.001
3	Immobilization, 10 h (n=10)	483±27	<0.9	421±9	<0.001	333±41	<0.05
	Vivarium control (n=9)	488±22		558±14		464±40	
4	Immobilization, 5 h, + 20 days in vivarium (n=5)	580±32	<1.0	692±79	<0.9	476±86	<0.3
5	Immobilization, 5 h, + 20 days of hypokinesia (n=5)	360±66	<0.02	578±39	<0.1	507±39	<0.2
6	Immobilization, 5 h, + 20 days in vivar. + 5-h immobilization (n = 5)	[illegible]47±29	<0.5	578±30	<0.05	410±69	<0.05
7	Immobilization, 5 h, + 20-day hypokinesia + 5-h immobilization (n=10)	446±41	<0.02	450±28	<0.001	365±35	<0.001
	Vivarium control (n=11)	563±31		679±23		566±23	

Histologically, the spleen of rats in the 1st group did not differ appreciably from control findings, with the exception of some increase in number of mature neutrophils in the red pulp. According to the data listed in the Table, there was no decrease in area occupied by the white pulp of the spleen. In rats of the 2d and 3d groups, unlike those in the 1st, we observed significant decrease in area of white pulp of the spleen (see Table), but it was not associated with death of lymphocytes and appearance of nuclear detritus in the lymphatic follicles. Intensive neutrophil infiltration was demonstrated in the red pulp of the spleen of rats in the 2d and 3d groups: large and small focal accumulations of mature neutrophils were encountered everywhere in the red pulp.

The histology of the thymus and spleen of rats in the 4th group did not differ from control findings.

In the 5th group of animals, the lobules of the thymus were somewhat reduced in size, the layers of interlobular connective tissue were slightly thickened, while the cortical substance of the lobules was reduced; a moderate amount of macrophages with clear cytoplasm was demonstrated in the cortical substance of the thymus. In the spleen of this group of rats, we demonstrated some decrease in size of lymphatic follicles and decreased cellularity, although no reliable decrease in white pulp area was noted (see Table). In the red pulp of the spleen, there was distinct inhibition of erythroid hemopoiesis, as indicated by the reduction in size and number of focal accumulations of immature erythroid cells. In addition, there was intracellular and extracellular accumulation of hemosiderin in the red pulp.

The histology of the thymus and spleen of rats in the 6th group differed little from that of the 1st group; the difference only consisted of the fact that, in the 6th group, there was a statistically reliable decrease in weight of the spleen and area of white pulp (see Table).

The most marked histological changes in the thymus and spleen were found in the 7th group of rats. Their thymus lobules were somewhat reduced in size, the interlobular connective tissue was slightly thickened and cortical substance of the thymus was constricted. Massive accumulations of nuclear detritus were found in the cortical substance of the thymus, and the amount thereof was greater in this group than in the 6th group.

The spleen of rats in the 7th group presented a distinct decrease in size of lymphoid follicles and area of white pulp (see Table). The decrease in size of lymphoid follicles occurred mainly due to loss of lymphocytes, as a result of which there was better demonstration of reticular stroma. In addition to the decrease in lymphocyte number, we encountered small accumulations of nuclear detritus in the follicles, which were not found in other groups. In this group of rats, there was neutrophil infiltration of the red pulp of the spleen, drastic decrease in number and size of sites of extramedullary erythropoiesis, intracellular and extracellular accumulation of hemosiderin.

The changes observed in rat lymphatic organs can be divided into two main types: the first includes changes such as massive breakdown of cortical lymphocytes of the thymus, hypoplasia of lymphoid tissue of the spleen, neutrophil infiltration of red pulp; the second refers to inhibition of erythroid hemopoiesis in the spleen and accumulation of hemosiderin in it. The first group of changes is a morphological manifestation of stress [10-12], whereas changes of the second type are not related to development of the reaction of the general adaptation syndrome, and they are consistently observed with muscular inactivity [13, 14].

During the hisotlogical examination of the thymus and spleen of rats that were submitted to acute immobilization stress, we were impressed by the differences in nature of reactions of the thymus and spleen to single exposure to the extreme factor. Thus, with acute stress, there was massive breakdown of lymphocytes in the thymus with subsequent development of the macrophage-phagocytic reaction (we cannot rule out the possibility of migration of lymphocytes from the thymus), whereas in the spleen no death of lymphocytes was observed, and the reduction of lymphoid tissue apparently occurred chiefly as a result of migration of lymphocytes [15-17]. There was much faster migration of lymphocytes from the spleen than elimination of destroyed lymphocytes from the thymus, as a result of which the weight of the spleen and area occupied by its white pulp were decreased as early as 10 h after onset of stress (2d and 3d groups); at this time there was still no decrease in weight of the thymus.

A comparison of the changes in the thymus and spleen of rats in the 1st and 2d groups, as well as the 3d group, warrants the statement that the changes in lymphatic organs due to stress reach maximum development 10 h after the start of immobilization of the animals and that 10-h immobilization stress does not worsen the severity of lesions to lymph organs, as compared to 5-h stress.

The absence of any changes in the thymus and spleen of rats in the 4th group, as compared to control findings, indicates that a 20-day period is quite sufficient for restoration of cellular composition and structure of lymphatic organs of rats submitted to acute immobilization stress.

As indicated above, the combination of 5-h immobilization and subsequent hypokinesia leads to hypoplasia of lymph organs. The integrity of typical structure of these organs warrants the belief that there is at least partial restoration of cellular composition of lymphatic organs following acute stress, in spite of hypokinesia. It should be noted that, along with the decrease in amount of lymphoid tissue, the loss of immature erythroid cells, which occurred due to inhibition of erythroid hemopoiesis, could also play a substantial role in reducing the weight of the spleen of rats submitted to hypokinesia.

The second 5-h period of immobilization 20 days after the first (6th group) led to development of changes in the rat thymus and spleen that were similar to those observed after single exposure to immobilization stress. At the same time, in rats submitted to immobilization a second time after 20 days of hypokinesia, the damage to lymphatic organs was appreciably greater than in animals submitted to immobilization a second time after spending 20 days in the vivarium, as manifested by the increase in number of disintegrated lymphocytes in the thymus and appearance of nuclear detritus in the lymphoid follicles of the spleen. Intensification of destructive processes induced by stress in lymph organs of rats following hypokinesia is perhaps attributable to a change in reactivity of the animals during long-term restriction of motor activity, since we know

that hypokinesia lowers resistance of the organism to subsequent extreme factors [18]. As shown by previous studies [1-3], there was massive breakdown of cortical lymphocytes of the thymus and moderate disintegration of lymphocytes in follicles of the spleen and parafollicular zone of lymph nodes, neutrophil infiltration of red pulp, hypoplasia of lymphoid tissue of the thymus and spleen, inhibition of erythroid hemopoiesis in the spleen and accumulation of hemosiderin in it in rats after flights aboard biosatellites. In view of the fact that such acute changes as breakdown of lymphocytes in lymph organs and neutrophil infiltration of the spleen reach maximum development about 10 h after the start of exposure to the stressor (results of the model experiment), there is every reason to believe that the development of analogous changes in rats that were exposed to weightlessness is related to acute gravitational stress, which occurred when the animals changed from weightlessness to earth's gravity. This is indicated by the absence of changes inherent in acute stress in lymph organs of rats exposed to artificial gravity of 1 G while aboard Cosmos-936, as well as the absence of lesions to lymph organs of rats submitted to accelerations in the ground-based experiment, which were equivalent to those that animals are subjected to during a biosatellite landing. As for acute changes in rat lymph organs that could be related to the effects on the animals of the extreme factors associated with lift-off and transition to weightlessness, there were barely traces thereof in lymph organs after 20 days of space flight, since there was restoration within this time of structure and cellular composition of lymph organs, as shown by our model experiment.

However, it would be wrong to believe that the involution of lymph organs observed in rats in the postflight examination was the result of gravity stress alone. According to the data obtained from the model experiment, prolonged hypokinesia leads to development of hypoplasia of lymphoid tissue. Consequenlty, restriction of motor activity of the animals during the space flight could also be one of the causes of involution of lymph organs. In order to determine whether weightlessness has a stressor effect on the body, inducing hypoplasia of lymphoid tissue, let us consider the results of weighing the thymus of rats flown about Cosmos-782 and Cosmos-936 artificial satellites of earth. The thymus weighed less in rats that were weightless during the space flight than in animals used in the synchronous ground-based experiment and animals exposed to artificial gravity during the flight. These data warrant the belief that expressly weightlessness is responsible for development of lymphoid tissue hypoplasia. Thus, the hypoplasia of the thymus observed in rats sacrificed several hours after the space flight is the result of chronic stress, the etiological factor of which is weightlessness.

In addition to lymphoid tissue hypoplasia, we consistently demonstrated inhibition of erythroid hemopoisis in the spleen of rats submitted to weightlessness, as well as accumulation of hemosiderin in it (as a result of intensive disintegration of lymphocytes). As shown by the model experiment, these changes are also observed in hypokinetic animals. Thus,

the insufficient muscular activity, which is inevitable as a result of restricted motor activity and weightlessness, is the cause of depressed erythropoiesis in the spleen of rats aboard biosatellites.

According to this study, the "accidental" [sic] involution of lymph organs observed in rats after long-term space flights is the consequence of two stresses, chronic and acute. Chronic stress arises in weightlessness and leads to hypoplasia of lymphoid tissue. Acute stress develops when the animals change from a state of weightlessness to earth's gravity ("gravity stress") and is associated with disintegration of lymphocytes in lymph organs, which aggravates substantially the hypoplasia of lymphoid tissue that appears under the influence of chronic stress due to weightlessness.

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UDC: 613.646

EFFECT OF HIGH AMBIENT TEMPERATURE ON HUMAN PERFORMANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 35-38

[Article by A. N. Azhayev, V. I. Zorile and A. N. Kol'tsov, submitted 6 Oct 78]

[English abstract from source]

Mental and physical capacity of men exposed to 30–35° at low humidity and to 25–30° at high humidity remained unaltered. The capacity of men exposed to 40–55 °C at 10–25 % of relative humidity and to 35–40 °C at 85 % of relative humidity declined

[Text] Workers in some occupations have to work at high ambient temperatures. It has been established that overheating has an adverse effect on functional systems of the body [1, 2]. However, the state of human performance [fitness for work, efficiency] when exposed for a long time to high temperatures inducing different degrees of overheating has not been adequately studied [3-6].

Our objective here was to determine the direction and severity of changes in physical and mental fitness of man in the course of many hours of exposure to high temperatures at low and high air humidity.

Methods

Two series of studies were conducted in a thermal vacuum chamber. In the first series, the air and wall temperature constituted 30, 35, 40, 45, 50 and 55°C and relative humidity was 10-25%; in the second series, the levels were 25, 30, 35 and 40°C, and 85%, respectively. The velocity of air movement in the chamber constituted 0.1-0.2 m/s. The tests of the first series lasted 6, 4.2 and 2.3 h at temperatures of 30-45, 50 and 55°C, respectively; in the second series they lasted 6 and 2 h at temperatures of 25-35 and 40°C.

With temperatures of 50 and 55°C and low air humidity, as well as 40°C at high humidity, the tests continued until rectal temperature rose to 38.4°C.

The subjects wore cotton T-shirts, shorts, a cotton fabric work-out suit, socks and shoes.

In all, we conducted 166 tests involving 17 essentially healthy males ranging in age from 24 to 40 years.

The studies were conducted in the fall and winter. Before starting the study, we trained the subjects in performing the tests until relatively stable results were obtained.

At the start of each hour of exposure to high temperature, we measured skin and body (rectal) temperature, heart rate (at rest and with measured exercise), time of simple sensorimotor reaction to a sonic stimulus, muscular strength and endurance of the hands according to the level of residual exertion after the liquid dynamometer held at the level of one-half the maximum muscular exertion for 1 min. Mental fitness was determined by the results of addition and substraction of numbers at a specified rate. In addition, we evaluated quality of control in the mode of compensatory tracking on a TUZO-3 instrument [7], in which the PSP-48 blind landing instrument served as a visual indicator. In the studies, we used sinusoidal input signals at a frequency of 0.1-0.15 Hz. The quality of control was assessed on the basis of determination of equivalent error by adding the values of different levels of errors for each 5 min of continuous work. In addition, the subjects performed standard flight assignments on a flight simulator. The quality of performance on the simulator was checked 4-5 times within 5-6 h. The subjects were exposed to an air temperature of 60°C for 40-60 min prior to each period of work on the simulator in order to maintain overheating conditions (rectal temperature of 38°C). We also determined the reserve capabilities of the subjects with regard to reception and processing of additional information and performance of motor acts on this basis. For this purpose, during the control process (main work), the subjects performed an additional motor task (depression of button) for 1 min in response to presentation of visual green and red signals, and we recorded the latency period of the motor reaction ("time of reaction involving choice").

We conducted 10 additional tests (with the participation of 5 people exposed to a temperature of 55°C), in which a suit was used that provided for water cooling of the entire body surface, with the exception of the face, hands and feet.

Results and Discussion

The results of the first series of tests revealed that there was no appreciable change in well-being of the subjects at ambient temperatures of 30 and 35°C. We only observed some facial hyperemia and wetness of the integument. Under these conditions, there was no substantial change in quality of performance of psychophysiological tests (time of simple sensorimotor reaction and time of reaction with choice), tracking, solving

arithmetic problems, as well as muscular force. At a temperature of 40°C, marked perspiration was already noted after spending 1 h in the chamber. Some subjects were listless and sleepy. At the tend of the tests, body temperature was 37.9±0.09°C. Upon further elevation of ambient temperature, there was an increase in perspiration, and it became profuse at 45°C. The sensation of listlessness, unwillingness to work and move was observed in most cases after spending 1 h in the chamber. Many subjects felt febrile in the 3d-4th h. Body temperature reached 38.2-0.15°C in the 6th h in the chamber.

There was reliable deterioration of fitness parameters with exposure to temperatures of 40-45°C. Maximum muscular strength diminished by 20% and tracking quality by 11.7-19.3%. There was a 19-27% increase in number of mistakes made in arithmetic problems. The latency period of response to green and red light signals increased by 17 ms ($P<0.05$) after spending 2 h in the chamber at a temperature of 45°C. After 4 h of exposure to the same temperature, there was also a statistically reliable increase in number of wrong reactions (by 66.6%). Under these conditions, there was no reliable change in time of simple sensorimotor reaction to a sonic stimulus.

At temperatures of 50-55°C, the subjects reported pulsation and pressure in the temples, heavy-headedness after spending 1 h in the chamber. This was associated with elevation of body temperature to 38.5±0.1°C. Maximum changes in muscular strength quality of tracking and solving arithmetic problems at temperatures of 50 and 55°C were observed in the 4th and 2d h, respectively, spent in the chamber. It should be noted that the change in tracking quality did not occur at the very start of control, but some time after beginning to work continuously, in the 3d-4th min.

Performance of measured physical exercise under overheating conditions led to significant increase in heart rate. Thus, we demonstrated an increase in heart rate by 20, 32 and 34/min at ambient temperatures of 45, 50 and 55°C, respectively. At the same temperatures, there was significant decrease in muscular strength following a static physical load.

There was virtually no change in quality of piloting the simulator after exposure to a temperature of 60°C (for 40-60 min). We merely observed some delay in executing the most difficult flight elements (simultaneously holding the specified bank and vertical speed, etc.).

The results of the second series of tests, which were conducted at a high level of air humidity, revealed that the well-being of the subjects was satisfactory at temperatures of 25 and 30°C. Body temperature constituted 37.3±0.06 and 37.5±0.05°C, respectively. We failed to demonstrate a reliable decrease in psychomotor reactions, muscle strength, quality of tracking and solving arithmetic problems.

At the very start of exposure to a temperature of 35°C, all of the subjects developed a feeling of listlessness, unwillingness to work or move. After spending 3 h in the chamber, there was a substantial deterioration of control quality in the tracking mode. Perspiration was profuse. In the 4th-5th h in the chamber, the subjects reported headache, sensation of pressure in the temples and occiput. Body temperature rose to 38.0±0.06°C. With further elevation of ambient temperature (to 40°C), these complaints were presented sooner, in the 2d h in the chamber. The subjects reported a febrile sensation, palpitations, paresthesia of the limbs and head region. Body temperature constituted up to 38.4±0.18°C. Considerable will power had to be applied to perform the work, and there was usually worsening of general well-being, intensification of perspiration, appearance of headache and sensation of pulsation in the temples. A change in work mode (subtraction of numbers projected on a screen instead of tracking) at temperatures of 35 and 40°C was associated with an increase in number of mistakes. At these temperatures, there was a reliable decrease in muscle strength.

Use of a water-cooled suit, in which the water temperature in the vinyl chloride tubing was held at 28-30°C, helped retain comfortable temperature conditions, high physical and mental fitness at ambient temperature of 55°C for the entire test period (4 h).

A comparative analysis of the changes in psychophysiological functions and subjective sensations revealed that fitness under the tested conditions depended not only on the external temperature, but duration of exposure to it and, consequently, degree of overheating of the body. At the start of exposure to high temperatures (after 15-20 min), there was some brief improvement of performance by the subjects, and this apparently occurs as a result of prevalence of excitatory processes and enlistment of adaptive capabilities of the body. Under the same conditions, not infrequently we observed some drop of rectal temperature (by 0.2-0.5°C). With increase in time of exposure to high temperatures and overheating, there was destabilization of piloting skills and decrease in efficiency. The studied parameters of psychophysiological functions did not change reliably in most cases.

Thus, the results of these studies revealed that exposure to ambient temperatures of 30-35°C at low air humidity and to 25-30°C at high humidity does not have an appreciable influence on thermal state, physical and mental fitness of man when performing light physical work involving energy expenditure of 70-100 W/m^2 (operator work). In such cases, the observed functional changes were indicative of the fact that man can adapt to such conditions. According to the classification of human heat states, the above microclimate conditions induce grade I overheating of the body (rectal temperature 37.6°C) and they are considered permissible [8].

At ambient temperatures of 40-55°C and humidity of 10-25%, as well as 35-40°C and 85% humidity, the changes in thermal state and performance

were not indicative of adaptation to these conditions. According to the classification of thermal states of man, these temperatures induce grade II overheating (rectal temperature 37.7-38.4°C) and they are considered to be at the maximum permissible level. In order to avoid disruption of adaptive mechanisms of heat regulation, they can be allowed for a limited time, with constant monitoring of functional state of the body's psychophysiological systems.

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DYNAMICS OF HUMAN EXTERNAL RESPIRATION AND BLOOD GASES UNDER THE COMBINED EFFECT OF HYPERCAPNIA AND HYPOXIA

M... w KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 38-41

[Article by L. Kh. Bragin, A. Ye. Severin, N. A. Agadzhanyan, G. A. Davydov and Yu. A. Spasskiy, submitted 6 Feb 79]

[English abstract from source]

In manned experiments gas mixtures with a step-by-step increasing pCO_2 and hypoxia of different levels were used. The experiments demonstrated variations in respiration, buffer systems and gases of the blood. The studies emphasized an important physiological role of a constant pCO_2 in blood, when breathing gas mixtures with a different O_2 content.

[Text] Both Soviet and foreign authors have mentioned the influence of hypoxia as a corrective agent to eliminate deconditioning, which occurs when man reduces his motor activity [1-3].

At the same time, it was shown that there is an increase in functional strain of the respiratory system with increase in level of hypoxia. Intensification of pulmonary ventilation causes a substantial drop of partial carbon dioxide tension in alveolar air and circulating blood which, in turn, has a "restraining effect" on intensity of ventilation required to maintain the p_AO_2 level [4].

It was suggested that CO_2 be added to inhaled air in order to reduce hypocapnia and, consequently, to also reduce the symptoms of acute hypoxia [5, 6].

However, it was subsequently demonstrated that addition of CO_2 to rarefied air to a state of normocapnia, with retention of the same partial oxygen tension in the alveoli, induced intensification of altitude sickness symptoms [7].

We submit here the results of studies of dynamics of external respiration, blood O_2 and CO_2 tension with different levels of hypoxia and "staggered" [step-by-step] increase in hypercapnia against the background of hypoxia.

Methods

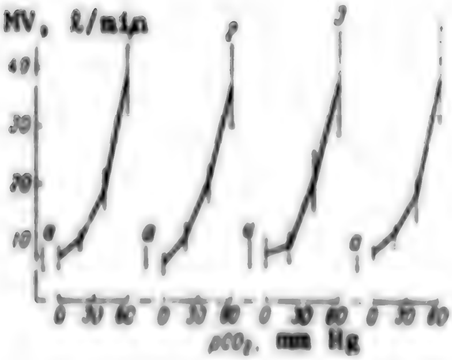
We conducted 4 series of studies with different gas mixtures at normal atmospheric pressure. In the first series, pO_2 of inhaled gas mixtures constituted 160 mm Hg, in the second, third and fourth it constituted 130, 100 and 70 mm Hg, respectively. We added CO_2 to each of these mixtures. The conditions of our tests involved elevation of pCO_2 in the inhaled mixture every 15 min, from 0 to 19, 38 and 57 mm Hg. In the 13th-15th min of breathing each of these hypercapnic-hypoxic mixtures, we measured the pulse rate, arterial pressure, P_aCO_2, P_aO_2, pH, respiratory quotient, CO_2 output, O_2 uptake, respiratory rate, minute volume (MV) of respiration. Exhaled air was collected in rubberized bags. We took an air sample from each bag and submitted it to analysis on an Ors-Fisher gas analyzer. We used a micro-Astrup instrument to measure pH and buffer components of blood, P_aO_2 and P_aCO_2. The other parameters were determined by the estimation method. In each series of studies there were eight participants. In all, we conducted 32 tests. The obtained data were submitted to statistical processing according to Student.

Results and Discussion

When breathing air, the respiratory rate of the subjects was 13-15/min, and it did not change appreciable with the change to a gas mixture with pO_2 of 160 to 70 mm Hg. Addition of CO_2 to the inhaled gas mixtures in an amount, with which pCO_2 constituted 19 mm Hg, did not induce an appreciable increase in rate of respiration. With pCO_2 of 38 mm Hg, the respiratory rate increased to 14-18/min, but this increase was also unreliable. It is only with inhalation of gas mixtures with pCO_2 of 57 mm Hg that there was a reliable ($P<0.05$) increase in respiratory rate to 18-23/min. The change from breathing air to breathing a hypoxic mixture with pO_2 of 70 mm Hg was associated with a statistically marked increase in pulmonary ventilation ($P<0.05$), which is consistent with the findings of a number of authors [8].

A comparison of pulmonary ventilation volume in subjects of all series of studies revealed that its mean level with the same degree of hypercapnia was quite similar, in spite of the different pO_2 levels in the mixtures. With pCO_2 of 19 mm Hg, pulmonary ventilation constituted 10-11 ℓ/min in all of the series. Elevation of pCO_2 in the inhaled gas mixtures to 38 mm Hg induced a reliable increase in MV, which increased to 18-20 ℓ/min BTPS at all pO_2 levels.

We demonstrated a correlation between pulmonary ventilation and degree of hypercapnia, while the presence of a "hypoxic component" in the pO_2 and pCO_2 combinations we used did not have a statistically marked effect on MV (see Figure).



MV with staggered elevation of pCO_2 against the background of different p) levels in inhaled air.
a) respiration of atmospheric air
1-4) pO_2 of 160, 130, 100 and 70 mm Hg, respectively

In all of the series of tests, there as an increase in O_2 uptake with elevation of pCO_2 in the inhaled gas mixtures to 57 mm Hg, but this was reliable only in the first series, where it constituted 344 40 mℓ/min STPD.

With such brief exposure to the gas environment, this probably occurs as a result of increased oxygen requirement due to the increase in energy expended on breathing and release of catecholamines in response to the "stressor" effect of CO_2, as well as because of the increase in $PaCO_2$ which is instrumental in output of O_2 as a result of a right shift of the curve of oxyhemoglobin dissociation (Bohr effect).

Ouput of CO_2 while breathing the same mixtures manifested, on the contrary, a tendency toward decrease. With pCO_2 of 57 mm Hg, CO_2 output dropped to 106-142 mℓ/min STPD. The respiratory quotient dropped to 0.5—0.72. The decline of the respiratory quotient when breathing mixtures with high CO_2 and low pO_2 is indicative of impaired stability of the correlation between CO_2 output and O_2 uptake.

Evidently, we can refer here to the effect of "locking" of endogenous CO_2 by exogenous CO_2 [9], as well as CO_2 binding (or more precisely binding of the HCO_3^- ion) by tissues [10].

In all series of studies, pCO_2 and pO_2 of peripheral blood underwent substantial change. P_aO_2 decreased, and the greater the O_2 shortage in inhaled air the more significant this decrease under the influence of hypoxia. In the fourth series, O_2 tension in blood dropped from 87 to 41 mm Hg. Addition of CO_2 to the mixtures increased pO_2 of blood. In the first series of studies, it rose to 93 mm Hg, i.e., it was 10 mm Hg higher than the initial level. In the second series, O_2 tension of blood showed virtually no difference from base levels (inhaling atmospheric air) with inhalation of a gas mixture with pO_2 or 130 mm Hg and pCO_2 of 57 mm Hg. In the third and fourth series, P_aO_2 rose by 20 mm Hg, but still was below base levels (due to the significant degree of hypoxia), constituting 77 and 61 mm Hg, respectively.

When breathing gas mixtures, blood CO_2 tension also presented typical dynamics. With pO_2 of 100 and 70 mm Hg, P_aCO_2 dropped from 39 to 36 and to 29 mm Hg, respectively. Addition of CO_2 to the gas mixtures, to 57 mm Hg,

increased blood CO_2 tension by 17-21 mm Hg, constituting 59, 55, 53 and 51 mm Hg in the first to fourth series, respectively.

A comparison of the data shows that only inhalation of a gas mixture with pO_2 of 70 mm Hg and pCO_2 of 0 mm Hg induced a substantial decline of P_aCO_2 as compared to initial levels. Addition of CO_2 to the inhaled gas mixture to a partial pressure of 19 mm Hg did not lead to a change in P_aCO_2 as compared to the initial level (breathing atmospheric air). Elevation of pCO to 38 mm Hg led to an increase in P_aCO_2, which was reliable only with pO_2 of 100 mm Hg in the inhaled gas mixture.

Finally, with pCO_2 of 57 mm Hg, we observed substantial saturation of peripheral blood with CO_2 at all levels of oxygen delivery to the body. Accumulation of CO_2 in the body and elevation of blood CO_2 tension induced about the same increase in blood acidity in all of the study series. pH constituted 7.33-7.35. There were also consistent dynamics to the buffer components of blood. The concentration of total bases had a tendency toward decrease in all series of studies: from 57.3-52 in the base state to 53.5-50 meq/ℓ when breathing gas mixtures where pCO_2 was 57 mm Hg. The concentration of actual bicarbonates decreased substantially, to 17.4-13.9 meq/ℓ, only when breathing gas mixtures with partial CO_2 pressure of 57 mm Hg; we failed to demonstrate any correlation between this and level of hypoxia.

There was a tendency toward decrease in amount of bicarbonates when scaled to standard conditions.

Finally, the index of compensation of CO_2 excess by buffer systems of blood ("base shortage") remained virtually unchanged in the first and second series, whereas in the third there was a reliable drop when breathing mixtures with pCO_2 of 38 and 57 mm Hg, to 1.4 and 0.5 meq/ℓ, respectively (versus the base level of 3.1 meq/ℓ). In the fourth series, we also observed a tendency toward decline of this parameter with increase in pCO_2 of inhaled gas mixtures, but only with the use of a gas mixture with pCO_2 of 57 mm Hg did this decline become reliable: from 3 meq/ℓ in the initial state to 1.12 meq/ℓ when breathing the above mixture. However, this decline should be deemed moderate, and it is indicative of the presence of respiratory acidosis with no signs of metabolic acidosis.

Thus, the dynamics of parameters of external respiration, blood buffer systems and gases when man is exposed to staggered levels of hypercapnia against the background of different levels of hypoxia are indicative of the need to take into consideration the important physiological role of a constant blood pCO_2 level when breathing gas mixtures containing different amounts of O_2.

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UDC: 612.176

FUNCTIONAL STATE OF THE CARDIOVASCULAR SYSTEM UNDER THE COMBINED EFFECT OF 28-DAY IMMERSION, ROTATION ON A SHORT-ARM CENTRIFUGE AND EXERCISE ON A BICYCLE ERGOMETER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 42-45

[Article by I. F. Vil'-Vil'yams and Ye. B. Shul'zhenko, submitted 19 Nov 78]

[English abstract from source]

The cardiovascular function of four test subjects exposed to 28-day "dry" immersion was examined before and after 6-day cycles of rotation on a short-arm centrifuge to provide 1-2 G_z, bicycle ergometer exercise, and their combination. An exposure to acceleration of 3 G_z on a 7.25 m arm centrifuge was used as a provocative test. The above countermeasures reduced but not eliminated entirely immersion-induced cardiovascular deconditioning. From this study a combined use of acceleration of 1-2 G_z on a short-arm centrifuge and bicycle ergometer exercise can be recommended as a countermeasure against cardiovascular deconditioning in weightlessness.

[Text] Rotating man on a short-arm centrifuge (SAC) is one of the possible means of preventing the effects of deconditioning in weightlessness [1-3].

Our objective here was to assess the functional state of the circulatory system and endurance of $+G_z$ accelerations after long-term exposure to "head-pelvis" accelerations in the range of 1-2 G on a SAC and exercise on a bicycle ergometer under conditions simulating the effects of weightlessness by means of immersion.

Methods

Four studies were conducted on healthy male volunteers involving 28-day immersion, based on the principle of "wet" submersion using highly elastic water-proof material [4]. The water temperature in the tank constituted 34±0.5°C, i.e., it was thermally neutral [5]. We used SAC rotation at different stages of immersion (see Table) in a progressively increasing mode. For 6 days, they were exposed for 2 days to each of the following levels of acceleration: +0.8, 1.2 and 1.6 Gz (at foot level) lasting 60 min

at a time, twice a day. The resulting G forces constituted 1.3, 1.6 and 1.9, respectively.

Schedule of tests during 28-day immersion

Day of immersion	SAC	Bicycle ergometer	Centrifuge with 7.25-m arm
Before immersion	−	−	+
1st-7th	−	−	−
8th	−	−	+
9th-14th	+	−	−
15th	−	−	+
16th-21st	−	+	−
22d	−	−	+
23d-28th	+	+	−
After immersion	−	−	+

The exercise on the bicycle ergometer involved a load of 600 kgf/min with 10 min of pedaling and 10 min of rest (3 such cycles for 60 min twice a day). In all, there were 96 rotations on the SAC, 48 of which were combined with pedaling. There were also 48 sessions of exercise on the bicycle ergometer that were not combined with rotation on the SAC. We generated +3Gz with an increment gradient of 0.2 G/s before immersion (7 days before), on the 7th, 14th, 21st and 28th days of immersion as a functional load test using a centrifuge with a 7.25-m arm. Rotation lasted up to 5 min before immersion, on the 7th and 28th days of immersion, and 1 min on the 14th and 21st days. We recorded the electrocardiogram (EKG) in the leads of (Neb) and arterial pressure (AP) in vessels of the ear lobe as modified in [6].

We recorded the EKG lead in the Neb leads, phonocardiogram, sphygmogram of the carotid artery, rheogram of the femoral artery using a 4RG-1A instrument, AP of the brachial artery using an AP-KTs instrument (Biofizpribor Plant) and elasticity of venous vessels of the arm by the method in [7] as modified in [8], before and after each preventive cycle. We calculated the heart rate (HR), systolic (SV) and minute (MV) volumes of the heart by the method of Bremzer-Ranke, and total peripheral resistance (TPR) using the formula of Poiseuille.

All of the data were submitted to variational processing according to Student. The differences were considered reliable with $P<0.05$.

Results and Discussion

There were phasic changes in mean parameters of systemic circulation during immersion (Figure 1). The most marked changes (usually within 10-20% of initial levels) were noted after 7 days of "pure" immersion, and they

were typical of the hypodynamia syndrome[9]: decreased SV and MV (from 93 to 82 mℓ and from 5.8 to 5.0 ℓ/min, respectively), increased TPR (from 1138 to 1512 dynes/s/cm^{-5}), elevation of diastolic AP (from 63 to 76 mm Hg) and drop of pulse AP (from 44 to 35 mm Hg). By the 14th day of immersion, HR decreased by 5/min. There was a tendency toward restoration of the main hemodynamic parameters to the base level under th nfluence of the preventive measures. On the 28th day of immersion, this tendency was significant for SV and pulse AP, as compared to the 7th day.

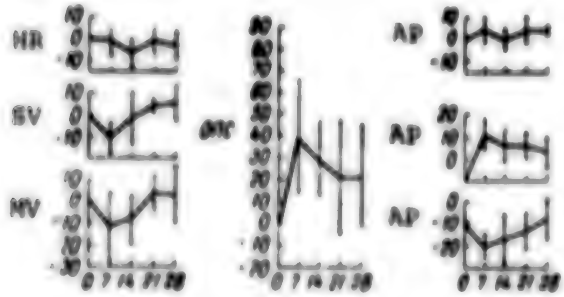

Figure 1.
Dynamics of relative changes in parameters of the cardiovascular system during 28-day immersion. X-axis, days of immersion; y-axis, parameters of cardiovascular system (Δ% of base levels)

There was significant increase in elasticity of vessels of the arm during immersion, which was indicative of substantial decrease in tonus of venous vessels (Figure 2). The changes in these parameters were the most marked (about 4-fold, as compared to the initial level) also on the 7th day of immersion.

The degree of change in mean values of parameters characterizing venous tonus diminished under the influence of preventive measures, although these changes were not usually statistically significant.

Endurance of +3Gz accelerations constituted a mean of 298±2 s for the entire group. After 7 days of "pure" immersion there was an overt tendency toward decrease in endurance to 130±87 s. Impaired vision in the form of a "gray" film or drop of AP in vessels of the ear lobe to below 40 mm Hg were the chief symptoms limiting endurance of G forces. On the 15th and 22d days of immersion after using preventive measures, all of the subjects endured 1 min of scheduled exposure to +3 Gz. Duration of final exposure to G forces after immersion for 28 days constituted 273±50 s, and it did not differ reliably from the duration of control rotations, which is indicative of diminished functional reserves of the circulatory system under the influence of the set of preventive measures.

A comparison of cardiovascular reactions to +3 Gz accelerations before and after 28-day immersion revealed that the postimmersion changes were more marked: increased synus tachycardia, drop of AP of ear lobe vessels, although it constituted a mean of 60 mm Hg in the 5th min of rotation, and it was above critical levels (Figure 3).

Thus, use of periodic rotation on the SAC (in the range of 1-2 G lasting for up to 60 min twice a day) combined with exercise on a bicycle ergometer

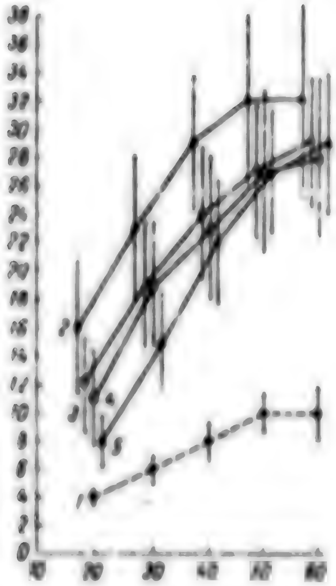

Figure 2.
Dynamics of elasticity of arm vessels during 28-day immersion. X-axis, pressure in cuff applied over arm (mm Hg) x-axis, elasticity of vessels of the forearm (in arbitrary units)
1) before immersion
2-5) 7th, 14th, 21st and 28th days of immersion, respectively

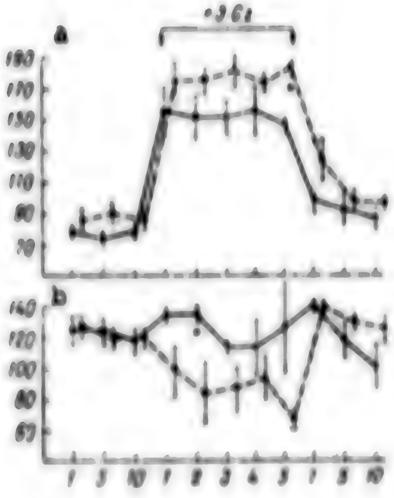

Figure 3.
Dynamics of parameters of the cardiovascular system with exposure to +3 Gz accelerations lasting for 5 min before and after 28-day immersion. X-axis, time of exposure (min); y-axis: a--HR (per min); b--AP in vessels of ear lobe. Asterisk indicates P<0.05 when comparing parameters before (solid line) and after (dash line) immersion

attenuated the effects of deconditioning of the cardiovascular system caused by prolonged immersion. These results are consistent with those of previous studies of preventive effects of periodic "gravity" loads at low levels simulated on a centrifuge with a medium-sized arm [1].

The preventive effect of the "gravity" loads combined with exercise on a bicycle ergometer was probably attributable to the complex influence of a number of factors, in particular, simulation of the hydrostatic blood pressure gradient along the great vessels of the body and simulation of a load on the skeletomuscular system. As we know, this stimulates mechanisms that regulate vascular tonus and attenuates signs of atrophy of the main antigravity skeletal muscles "due to disuse" [10]. Evidently, the increased expenditure of energy related to exercise was also important, and perhaps it had some influence on MV dynamics during immersion in view of the close correlation between these parameters [11]. Probably, the function of the peripheral muscle pump while pedaling on the bicycle ergometer also played a role; this, as we know, is involved in increasing venous return of blood

to the heart and when associated with exposure to low levels of +Gz accelerations and the magnitude of exercise we selected (600 kgf/min) increases venous return to the heart, cardiac output and pulmonary flow, and has a tonic effect on the cardiovascular system [12].

These studies also revealed that the effects of deconditioning of the cardiovascular system under the influence of the tested preventive measures were not completely eliminated. As can be seen from our findings, diminished tonus of capacitance vessels, which was perhaps related to decreased tonus of the adrenosympathetic and muscular systems during immersion, may be one of the possible causes of this phenomenon [13].

The obtained data warrant recommendation of the combination of rotation on a SAC in the range of 1-2 G and physical exercise on a bicycle ergometer as a means of preventing deconditioning of the cardiovascular system when in weightlessness.

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UDC: 612.13.014.477-08:615

PHARMACOLOGICAL ANALYSIS OF PHYSIOLOGICAL MECHANISMS OF ORTHOSTATIC HEMODYNAMIC STABILITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 45-49

[Article by L. I. Osadchiy, submitted 30 Jan 78]

[English abstract from source]

In urethane anesthesized cats, securinine brought about a distinct increase in compensatory reactions of arterial pressure and cardiac output during an upright tilt at [illegible]. The experiments also showed a substantial increase in compensatory recovery of the volume velocity of circulation in the posterior vena cava. Myorelaxant induced arrest of contractile function of skeletal muscles prior to securinine administration reversed compensatory reactions of arterial pressure and cardiac output during tilt test.

[Text] The increased interest in recent years in questions of stability and gravity loads is related to the need to develop preventive measures to lower the intensity of reactions when changing from weightlessness to earth's gravity. This also applies to gravity loads with orthostatic reactions that occur after spending a long time in horizontal position without exercise. The existing facts indicate that there is a possibility of preventing hemodynamic orthostatic reactions following hypodynamia by means of pharmacological agents that stimulate the central nervous system [1] and circulatory system [2].

On the other hand, there are data pertaining to adaptive reactions of the circulatory system to orthostatic factors [3-6]. It was previously established [5] that compensatory arterial pressure reactions are determined in cats in the orthostatic test chiefly by the vascular component of the systemic reaction to orthostasis. Moreover, it was found that the baroreceptive reflexes, which are of substantial significance to these compensatory reactions, occur mainly by means of change in tonus of peripheral vessels.

In view of the foregoing, it was deemed important to explore the physiological mechanisms at the basis of compensatory hemodynamic reactions to

orthostastatic position, which are stimulated by pharmacological agents, in particular securinine, which increases orthostatic stability of man [1]. This product is known as a central nervous system stimulant of plant origin, which has a strychine-like action [7].

Methods

Experiments were conducted on cats under urethan anesthesia (1.0 g/kg). The orthostatic test (OT) was performed by turning the table to 45° from the horizontal axis with the head up for 1-3 min. Arterial pressure (AP) was measured in the carotid artery with a mechanotronic electromanometer [8]. In some experiments, a similar sensor was used to record central venous pressure (CVP) in the anterior vena cava and, through a catheter, in the external jugular vein. The external tips of the catheter were on the pivot shaft [axis of rotation] of the table to avoid artefacts when there was a change in correlation between levels of the catheters and pressure sensors. The cuff sensor of an RKE-1 electromagnetic flowmeter [9] was used for continuous recording of cardiac output; this device records the volumetric blood flow rate in the ascending aorta. Volumetric blood flow rate in the posterior vena cava was recorded with the flow-type sensor of an RKE-1 electromagnetic flowmeter inserted in the vessel that carries blood from the posterior vena cava to the right atrium [10]. All of the processes were recorded on an USChV-8 ink-writing oscillograph, and the data were submitted to statistical processing using Student's paired t-test.

Results and Discussion

In the first series (13 experiments) we studied the effect of securinine on systemic hemodynamics in order to determine the range of doses that alter the activity of the cardiovascular system (Table 1).

It was established that, in a dosage of 0.25 mg/kg, securinine elicited reliable pressor changes in AP in only half the cases (out of 26), and it did not affect cardiac output in any case. Such a dosage of securinine may be considered the threshold for the circulatory system. Increase in dosage to 0.5 mg/kg was associated with appearance of pressor reactions in 20 out of 23 cases, as well as reliable increase in cardiac output in the same 20 cases. Further increase in dosage to 1.0 mg/kg led to an increase in amplitude and duration of pressor AP reactions and cardiac output changes in all 16 cases, and this was associated with marked general motor activity of the animal.

It should be noted that, in our experiments, we demonstrated greater sensitivity of the circulatory system to securinine (by about 3-4 times) than in previously published articles [7].

Although we cannot derive a definitive conclusion about the mechanism of action of securinine on systemic hemodynamics on the basis of the reported

data, it can be assumed that securinine affects the circulatory system, and its action depends on both its direct influence on vasomotor centers and changes in muscular activity of central origin. It is known that the latter could lead to involvement of the "muscular pump" [10, 11] in the reaction, which expells blood from the veins to the heart and thereby increases cardiac output and AP. Moreover, we cannot rule out the peripheral effect of securinine on smooth muscles of the vascular walls.

Table 1. Changes in AP and cardiac output of cats given different doses of securinine (M±m)

Securinine dose, mg/kg	Number of cases	AP, mm Hg			Cardiac output, mℓ/min		
		base level	Δ_{max}	P	base level	Δ_{max}	P
0.25	13	130	+4.8±1.5	<0.05	310	+12±7.2	<0.05
0.5	20	127	+8.2±1.7	<0.05	288	+22±6.2	<0.01
1.0	16	122	+12.4±2.8	<0.01	272	+32±7.8	<[illegible]

All of the above mechanisms are directed toward increasing vascular tonus and output of the heart.

In the second series (14 tests) we studied the effect of securinine on compensatory reactions of systemic hemodynamics, which develop in response to a positive gravity load under OT conditions.

It was established that administration of securinine in a dosage of 1.0 mg/kg was associated with reliable change in compensatory reactions of the cardiovascular system in 19 cases (out of 28) (Table 2). While AP dropped by a mean of 20% of the initial level in response to orthostatic conditions and maximum restoration of AP during the OT period reached 25% before giving securinine, after administration of this agent the latter index constituted 70% of the maximum AP decline, which constituted 16% of the base level. Before administration of securinine, cardiac output decreased by a mean of 22% of the base level, while recovery was virtually absent in the OT period; after giving securine, the last mentioned parameter constituted 70% of maximum AP decline, which amounted to 16% of the base level. Before giving securinine, cardiac output dropped by a mean of 22% of the base value, and there was virtually no restoration during the OT; after giving securinine, the maximum decline of cardiac output constituted 16% of the initial level and restoration was 64% of maximum decline of cardiac output.

We recorded volumetric flow rate in the posterior vena cava in seven experiments to define the dynamics of venous return to the heart during OT. We found that, while venous influx, which initially dropped by a mean of 48%, failed to demonstrate a tendency toward compensatory restoration before giving securinine, after the latter it constituted 72% of the maximum

decrease in venous influnx in the posterior vena cava. The latter corresponds in phase to the compensatory change in AP and CVP observed in these tests, as well as the compensatory cardiac output reactions demonstrated in the experiments described above.

Table 2. Effect of securinine (1.0 mg/kg) on orthostatic stability of systemic hemodynamics (AP and cardiac output) of cats

Experimental conditions	AP, mm Hg			Cardiac output, ml/min		
	base level	Δ_{20}	Δ_{60}	base level	Δ_{20}	Δ_{60}
Before giving securinine	142±12	−28±2.6	−21±3.2	268±18	−50±7.4	−56±6.4
After giving securinine	152±8	−24±4.2	−8±2.5	284±12	−45±6.6	−16±4.3
P	>0.05	>0.05	<0.01	>0.05	>0.05	<0.01

Note: Mean values of 14 tests are given. Δ_{20} and Δ_{60} refer to changes in the 20th and 60th s, respectively, of 3-min OT.

Evidently, the mechanism of restoration of AP during the OT is determined both by intensification of recovery of venous influnx to the heart, which in turn leads to increased cardiac output, and increased vascular tonus. The latter could lead to a greater AP reaction, not only as a result of increase in resistance of resistive vessels, but by virtue of involvement in the compensation process of tonus of capacitive vessels [5, 6, 10], with subsequent increase in CVP and intensification of venous influx to the heart, which leads to an increase in cardiac output.

Consequently, securinine can affect compensatory AP reactions via both mechanisms, cardiac and vascular, and interaction between these factors was confirmed in an analysis of a number of other systemic circulatory reactions [10]. However, in view of the more marked vascular component of systemic reactions to orthostatic position [7], there is every reason to believe that the cardiac output changes are secondary to the primary compensatory changes in vascular tonus.

In view of the strychnine-like central effect of securinine and related increase in motor activity of the animals, we studied the influence of involvement of contractile activity of skeletal muscles on the abovementioned effect of enhancement of orthostatic stability by securinine.

To rule out contractile activity of muscles, we used the muscle relaxant lysthenon in a dosage of 2 mg/kg, which completely paralyzes skeletal muscles of the limbs and respiratory muscles in the 15th-20th min. Lysthenon was given just prior to securinine (in a dosage of 1.0 mg/kg).

in seven tests (third series), it was demonstrated that, while the maximum compensatory reaction of AP during the OT reached a mean of 28% of the maximum AP drop prior to exclusion of contractile activity of skeletal muscles, 3 min after giving the myorelaxant followed by administration of securinine there was no recovery of AP in any of the tests. As for the cardiac output reaction, securinine did not induce compensatory changes in the case of preadministration of lysthenon, although, as indicated above, this agent stimulated compensatory reactions of both AP and cardiac output.

The obtained findings warrant the conclusion that motor activity of skeletal muscles, which occurs in response to the OT [6], plays a substantial role in the mechanism of maintaining orthostatic stability by enhancing compensatory changes in systemic hemodynamics. Elimination of muscular activity virtually eliminates compensatory influences under orthostatic conditions which were stimulated by securinine. This is probably related primarily to involvement of the "muscle pump," in view of intensification of contractile activity of skeletal muscles.

Thus, it was demonstrated that securinine can have a preventive effect, by enhancing orthostatic stability of the organism. This is consistent with the above data concerning the increase in orthostatic stability after administering securinine to individuals following hypodynamia [1]. The fact that orthostatic stability increased in individuals during many hours of immersion as a result of being given small doses of vasopressin [6] may serve as a confirmation of this. Studies were conducted that established that adrenostimulators increase human stability with the head tilted upward at an angle of 45° [12]. We know of studies that demonstrated an increase in resistance to gravity loads after administration of agents capable of increasing vascular tonus [13].

In conclusion, it should be noted that pharmacological analysis of the mechanisms of orthostatic stability permits demonstration of the physiological mechanisms at the basis of compensatory reactions, which are related to activation of the cardiovascular and muscular systems.

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UDC: 612.822.3-06:612.766.2

BIOELECTRIC ACTIVITY OF THE HUMAN BRAIN DURING AND AFTER 182-DAY ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 49-54

[Article by T. N. Krupina, Kh. Kh. Yarullin and D. A. Alekseyev, submitted 22 Apr 78]

[English abstract from source]

Cerebral bioelectric activity of 18 healthy test subjects, aged 31–40, was examined during and after their 182-day head-down tilting. The test subjects were divided into a group that performed countermeasures (exercise, muscle stimulation) against hypokinesia-induced disorders and a control group. During the study EEG changes were most pronounced in the controls: α-rhythm amplitude, frequency and index decreased, slow wave frequency reduced, whereas index of zonal differences and amplitude of β- and slow waves increased. Phasic changes in the central nervous system excitability in response to a flickering light of 6–25 cps were found. Typical changes in spontaneous EEG during a 3 min pulmonary hyperventilation test were enhanced. The study gives evidence that the dynamics of spontaneous EEG as well as cerebral bioelectric activity in response to flickering light and pulmonary hyperventilation are important indicators of the cerebral function, especially of the cortical activity decrease

[Text] One of the most pressing problems of space medicine is to preserve a high degree of performance by cosmonauts during exposure to weightlessness for a long time. It is of great practical importance to study the functional state of the central nervous system during long-term space flights and, consequently, prognostic determination of its capabilities and reserves from these standpoints.

Our objective here was to make an electroencephalographic study of the functional state of the human brain during simulation of the physiological effects of weightlessness by means of bed rest in antiorthostatic (-4° tilt of head) position, as well as to assess the efficacy of preventive and rehabilitation measures.

Methods

Studes of 182-day antiorthostatic hypokinesia (ANOH) were conducted on 18 men ranging in age from 31 to 40 years following a thorough clinical examination. We formed 3 groups of subjects with 6 men in each: the first consisted of individuals submitted to ANOH with the use of a physical load involving a total expenditure of energy of about 1800 kcal over a 4-day cycle; the second consisted of men exposed to ANOH with half the physical load of the first group, and the third was a control group. We used lower body negative pressure (LBNP) and fluid-sodium correction as additional preventive measures for the first and second groups. In addition, electric stimulation of the muscles was performed in the first group. The article of L. I. Kakurin et al. [1] provides more details on the set of preventive measures. ANOH conditions are analogous to those described by A. D. Voskresenskiy et al. [2].

The electroencephalogram (EEG) was taken in the background period, 4th, 16th, 32d, 61st, 96th, 128th and 176th days of ANOH, 4th, 15th, 30th and 50th days of the rehabilitation period, from 8 symmetrical points on the scalp (forehead, center, temple, occiput) in bipolar and monopolar variants, on a portable 8-channel electroencephalograph, at rest (spontaneous EEG) and during functional tests (rhythmic photostimulation at a frequency of 6-25 Hz and pulmonary hyperventilation for 3 min). Along with visual evaluation of the EEG of the right central and occipital lead at rest and with hyperventilation, we determined the amplitude, frequency and index of α-, β-, θ- and δ-activity, calculated (in arbitrary units) the index of regional differences (ratio of index of α-rhythm in the right central occipital lead to index of α-activity in the frontocentral lead). These parameters were submitted ot statistical processing using the t criterion. The severity of diffuse changes in bioelectric activity of the brain was assessed according to Ye. A. Zhirmunskaya [3]. The sign criterion was used for statistical processing of the results of the test with rhythmic photostimulation [4]. The variants of responses with adoption of rhythm, change therein, depression of main activity and its synchronization were summated separately for two groups of frequencies: 15, 20, 25 and 6, 9, 12 Hz.

Results and Discussion

The spontaneous background EEG was in the normal range in 13 subjects, while mild (1 subject in the second and 1 in the third group), or mild and moderate diffuse changes (3 subjects in the first group) in bioelectric activity of the brain were noted in the rest. In addition, during hyperventilation there were mild diffuse changes lacking in the spontaneous EEG in another 3 subjects of the second group.

Thus, the background studies revealed that the groups were not homogeneous according to EEG parameters. The control group was characterized by the greatest homogeneity and least changes in bioelectric activity of the brain,

as compared to the first and second groups. In 5 subjects of the third group, bioelectric activity of the brain was in the normal range, and only 1 subject was an exception: against the background of a "desynchronized" EEG, he presented bursts of high-amplitude (up to 60 μV) β-activity at a frequency of 18 Hz.

Maximum heterogeneity and EEG changes in the background studies were noted in the first group. They consisted of disorganization of α-rhythm and build-up of slow activity during hyperventilation in 2 subjects, and presence of high-amplitude (70 μV, 3 Hz) diffuse, polymorphic δ-activity, as well as diffuse θ-activity (up to 40 μV) against the background of marked disorganization of main rhythm in 1 subject.

In 5 subjects of the second group, the spontaneous EEG was in the normal range, while there was dominance of β-activity (18 Hz, 25 μV and 30 Hz, 50 μV) against the background of disorganized α-activity in 1 subject. Mild and diffuse changes in bioelectric activity of the brain appeared in 3 subjects during hyperventilation.

In the control group, in spite of greater homogeneity and less marked changes in the background EEG, the changes in EEG parameters were found to be the most significant during ANOH. The amplitude of α-activity on the spontaenous EEG increased to 66.5±17.5 μV on the 4th day of ANOH (versus background of 55.8±14.9 μV) and held at this level up to the 96th day of ANOH (66.7±17.5 μV), after which it diminished to considerably below the background level (32.7±10.5 μV, $P<0.05$). The changes in amplitude of α-rhythm were less marked in the second group, but they retained the same tendency: the amplitude increased from 45.0±7.0 μV in the background to 60.0±14.0 μV only on the 16th day of ANOH, and after the 32d day it gradually decreased without reaching background levels, even on the 176th day (46.8±7.4 μV). In the first group, there was unreliable change in amplitude of α-rhythm during ANOH.

There was gradual decrease in dominant activity on the spontaneous EEG during ANOH, and it was the most significant in the first (from 10.2±0.3 Hz in the background to 8.9±0.8 Hz on the 176th day of ANOH, $P<0.05$) and second (from 10.1±0.2 to 9.3±0.3 Hz, $P<0.05$) groups. The α-rhythm index dropped (from 30.8±8.8 to 16.6±8.8%, $P<0.05$, in the first group; from 55.0±11.4 to 30.0±7.0%, $P<0.05$, in the second and from 61.6±14.0 to 32.5±10.5%, $P<0.05$, in the third).

Visual analysis of the spontaneous EEG revealed that diffuse β-activity was the most marked at the start (4th and 16th days) and end (176th day) of ANOH. In addition, there were segments of low-frequency (14-25 Hz), high-amplitude β-rhythm throughout the ANOH period. On the 176th day of ANOH, the amplitude of β-activity increased to 36.6±7.8 μV in the third group, 32.3±4.7 μV in the second and 22.6±1.8 μV in the first ($P<0.05$).

Regional differences, which were the most marked in the third group, were noted as a result of decrease (and often disappearance at the end of ANOH) in θ-activity of the anterocentral parts of the brain. The index of zonal differences on the 176th day of ANOH rose to 4.9±1.2 in the third group, 3.5±1.2 in the second and 3.0±0.7 in the first.

Slow-wave amplitude increased during ANOH, while frequency diminished the most in the third group. The amplitude of slow activity on the 176th day of ANOH increased to 45.0±7.0 μV ($P<0.05$) in the third group, 33.5±4.7 μV ($P<0.05$) in the second and 30.8±2.6 μV ($P>0.05$) in the first. The frequency of slow activity in the third group began to decline as early as the 16th day of ANOH (5.7±0.3 Hz) and constituted 4.5±0.3 Hz ($P<0.05$) on the 128th day of ANOH. In the second group these changes were less marked: the frequency of slow activity began to decrease on the 32d day of ANOH (5.1±0.3 Hz) and constituted 4.5±0.2 Hz on the 176th day of ANOH ($P<0.05$). There was no change in frequency of slow activity in the first group throughout the period of ANOH.

The test with rhythmic photostimulation demonstrated intensification of the phasic reaction of bioelectric activity of the brain to flashes of light during ANOH. On the 4th day of ANOH there was an increase in number of responses with adoption of photostimulation rhythm at a frequency of 15-25 Hz and synchronization of α-activity at frequencies of 6-12 Hz. These changes were the most marked in the third group ($P<0.05$). In two subjects of the first group who presented changes in background rhythm during photostimulation at a frequency of 15 Hz we observed appearance of sharp waves (in P-v, 36 years of age, on the 4th day of ANOH) and bilaterally synchronous paroxysmal discharges of 7/s with amplitude of up to 100 μV (in G-v, 37 years old, on the 16th day of ANOH).

During the second half of the ANOH period, there was a change in structure of bioelectric reactions of the brain to flashing light: upon stimulation at a frequency of 15-25 Hz the number of responses with adoption and change of rhythm diminished while the number of responses with depression and synchronization of activity increased. Conversely, at frequencies of 6-12 Hz, there was an increase in number of reactions with adoption and change in rhythm. Marked phasic changes in structure of bioelectric responses of the brain (in the frequency ranges of 15-25 and 6-12 Hz) were inherent in the second group ($P<0.05$).

The changes on the EEG during 3-min hyperventilation during ANOH presented the same direction as spontaneous bioelectric activity, and they were the most marked in the third group. There was appearance of paroxysmal, bilaterally synchronous slow activity (5-6 Hz, up to 200 μV) during hyperventilation in 5 subjects (1 in the second group, 2 in the first and 2 in the third), in all cases associated with changes in the background EEG. In these subjects, paroxysmal activity was recorded on the 4th day of ANOH, 4th and 15th days of the recovery period, less often on the 16th and 176th days of ANOH, 30th and 50th days of the rehabilitation period, and it

was marked primarily in the central regions of the cerebral cortex. In 3 subjects with changes in the background EEG (1 from each group), there was appearance of locally impaired type of bioelectric brain activity with unilateral demonstration of a focus of slow activity (up to 70 μV) on the 61st, 96th, 128th and 176th days of ANOH, as well as in the rehabilitation period at the height of hyperventilation, while hyperventilation was associated at the above times with motor restlessness and complaints of headache, dry mouth, sensation of numbness in the arms and legs.

There was a significant difference between bioelectric activity of the brain in the recovery period and the background. The amplitude, frequency and index of α-activity on the spontaneous EEG were below background levels ($P<0.05$) throughout all 50 days of the recovery period, while the index of zonal differences, amplitude of β- and slow activity were above base levels ($P<0.05$). These changes were the most marked in the third group and the least marked in the first. Throughout the entire recovery period, the number of responses with rhythm adoption to rhythmic photostimulation at a frequency of 15-25 Hz was greater than in the background ($P<0.05$), with synchronization of α-activity in the range of 6-12 Hz. In 3 subjects with changes in the background EEG, we observed bilaterally synchronous paroxysmal activity, manifested mainly in the central zones of the cerebral cortex, up to the 50th day of rehabilitation during hyperventilation. The localized nature of the EEG persisted on the 50th day of the recovery period in 1 subject (second group).

As can be seen from the above findings, prolonged ANOH led to intensification of mild pathological signs observed in some subjects prior to the study. Considering the different degree of background changes in bioelectric activity of the brain (the least in the third group and the greatest in the first) and the submitted results, it can be concluded that the greatest changes in bioelectric activity of the brain during ANOH were noted in the third group and the least in the first.

The results of the studies during the recovery period revealed that the EEG was closest to the background in the first group and farthest in the third. The incomplete recovery of EEG parameters indicates the severity of changes in bioelectric activity of the brain observed during ANOH, on the one hand, and the prolonged period of recovery, in spite of the set of therapeutic and rehabilitation measures used, on the other.

We can assess the functional state and capabilities of the central nervous system to some extent on the basis of the distinctive changes in main parameters of bioelectric activity of the brain [5-10].

Increased activation of the cerebral cortex is reflected on the EEG by an increase in β-activity and occasionally appearance of sharp waves and spikes [5, 7, 9-12]. During rhythmic photostimulation, the range of adopted rhythms shifts in the direction of higher frequencies, while in the range of low ones there is an increase in response with synchronization of α-activity [7, 11, 13, 15].

As shown by the results of this study, there was an increase in number and amplitude of β-waves on the 4th, 16th and 176th days of ANOH and in the recovery period; upon photostimulation, some of the subjects presented sharp waves and bilaterally synchronous paroxysms of θ-rhythm, as well as change in structure of bioelectric responses of the brain to flashing light: greater adoption of rhythm and change therein in the range of high frequencies, as well as synchronisation of α-rhythm in the low-frequency range. The presence of these changes in spontaneous bioelectric activity of the brain during functional loads at the above stages of hypokinesia and absence thereof in the middle and at the end of the ANOH period apparently indicates an increase in excitability of the central nervous system at these times, not only with reference to the cerebral cortex, but mesodiencephalic structures.

The heightened excitability of the central nervous system, as demonstrated by the REG and EEG dynamics in the second and third groups of subjects, during the first week of ANOH was apparently attributable to early change in regulatory mechanisms of supplying blood to the brain under the unusual ANOH conditions [16]. On the first day of the recovery period, it was apparently induced by development of reactive hyperemia of the brain in response to ischemia during the last weeks of ANOH and general reaction to termination thereof [17-21].

The phasic changes we observed in bioelectric activity of the brain during ANOH were analogous to those previously described [19, 21].

Studies of the use of pharmacological agents [9, 22], internal and supraliminal inhibition [5, 11, 13, 23, 24], diffuse sleep [6, 7, 12, 14, 25, 26] and narcotic [27] inhibition revealed that prevalence of inhibitory processes in the central nervous system is reflected on the EEG by slowing of main rhythms, decreased amplitude of electric oscillations, increased diffuse, polymorphic, slow activity, as well as decrease in its frequency.

It was previously demonstrated that during sleep the reaction of repeating the rhythm of light flashes had a lower frequency than when awake [25]. In the presence of deeper anesthesia, the evoked reactions to rhythmic stimulation are much less marked than in the background tests [27]. In other words, there is prevalence of low-frequency changes in rhythm when there is a low level of cortical activation in response to flashing light, whereas in the range of high frequencies there is either minimal or no adoption of rhythm [13, 28].

Consequently, analogous EEG changes during the second half of the ANOH period can apparently be attributed to prevalence of inhibitory states in the central nervous system related to increased general asthenization of the body [17, 18]. The latter, as well as impairment of cortical-subcortical correlations, with prevalence of inhibitory processes in the cortex, probably explains the rapid fatigability of the subjects during the functional tests, their drowsiness at the end of the ANOH period, as well as appearance

of locally impaired EEG in some of the subjects, with a unilateral focus of high-amplitude polymorphic δ-activity. As we know, there is prevalence of high-amplitude slow oscillations of potential in the presence of diffuse sleep inhibition [6, 7, 25].

Appearance of locally impaired bioelectric activity of the brain could also result from cerebral circulatory disorders. This possibility is indicated by the data of Kh. Kh. Yarullin et al. [29], who observed that there was an increase in phasic changes and appearance of asymmetry of rheoencephalographic parameters of pulsed circulation and vascular tonus with increase in duration of hypokinesia.

The obtained data indicate that the dynamics of the spontaneous EEG (amplitude, frequency, rhythms), as well as changes therein in response to flashing light and hyperventilation, are important indices for evaluation of the functional state of the brain and, particularly, diminished cortical activity.

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UDC: 612.465-06:612.766.2

MORPHOMETRIC ANALYSIS OF GLOMERULES AND JUXTAGLOMERULAR SYSTEM OF THE RAT KIDNEY IN THE COURSE OF EXPERIMENTAL HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 54-57

[Article by I. P. Chernov and A. G. Gaffarov, submitted 30 Jan 78]

[English abstract from source]

In the hypokinetic study a certain correlation between variations in the means of the volume of cortical and juxtamedullary glomerules and the function of the juxtaglomerular apparatus has been established. It is hypothesized that at early hypokinesia renal vascular changes are nonspecific. The phenomenon of renal retention of fluids and electrolytes is explained in terms of a simultaneous increase in the renin-angiotensin activity and 11-hydroxycorticosteroid content in plasma.

[Text] Importance is attributed to impairment of fluid-electrolyte metabolism in the pathogenesis of the hypokinetic syndrome [1-3]. These disturbances are based on changes in regulatory influence of the nervous and humoral systems on the kidney, general and renal hemodynamics [4-7]. It is quite obvious that we could not understand completely the nature and severity of changes in renal function without studying the structural changes associated with them.

We have tried to analyze here the state of renal vessels under hypokinetic conditions by means of histological and morphometric methods, and to compare the demonstrated changes to activity of cells of the juxtaglomerular system (JGS), which is directly involved in regulation of hemodynamics, transport of fluid and electrolytes.

Methods

We conducted this study on 70 male mongrel rats with an initial weight of 150-170 g. We created hypokinesia by keeping the animals in box-cages. The animals were decapitated after 3 h, and on the 1st, 3d, 5th, 10th, 20th and 30th days of the experiment. An ocular micrometer was used to measure the short (B) and long (L) diameters of cortical and juxtamedullary glomerules on kidney sections from experimental and control rats. We

differentiated between these glomerules according to their topographic location [8] and size of afferent and efferent vessels [9]. We counted up 50 cortical and 50 juxtamedullary glomerules on several sections referable to 6 animals at each examination. The volume (in cubic micrometers) was calculated with the following formula:

$$V = \frac{\pi}{6} (LB)^{3/2}$$

To obtain a more graphic expression of the effect of hypokinesia, the absolute mean volume was expressed as a percentage of the control, taken as 100%. We assessed the JGS by determining granularity of its cells stained according to Bowie and then calculating the juxtaglomerular index (JGI). On the basis of the data in the literature [10], we made a distinction between four grades of granularity. The calculation was made with the following formula:

$$JGI = \frac{1n_1 + 2n_2 + 4n_3 + 8n_4}{N},$$

where n_1, n_2, n_3 and n_4 refer to the number of JGS cells with each grade of granularity, N is the total number of glomerules in the preparation [11]. Fluorimetry was used [12] to determine 11-HOC [hydroxycorticosteroids] in blood plasma at different stages of hypokinesia. The results were submitted to processing by the method of variational statistics [13]. Reliability was determined with the criterion of Student.

Results and Discussion

At the early stages of hypokinesia (3 h and 1 day) there were morphological signs of redistribution of blood in the kidney. They consisted of spasm of small arteries and arterioles of the cortex, considerable dilatation and plethora of arcuate veins and straight vessels of the medullary layer. There was a statistically significant decrease in volume of subcapillary glomerules and those of the external cortical layers, while those of the juxtamedullary zone were reliable greater in volume than the control level (see Table). By the 3d experimental day, both the medullary layer and cortex were plethoric, and not only vascular glomerules of renal corpuscles, but the capillary system of the tubules were subject to marked dilatation. The medullary vessels remained dilated. On the 5th day of hypokinesia, the capillaries of the juxtamedullary glomerules were still plethoric, whereas there was prevalence of glomerules with collapsed capillaries in the cortex. Thereafter (10th, 20th, 30th days) there was a tendency toward decreased plethora of capillaries, as well as cortical and juxtamedullary glomerules.

At the first two examinations, the morphological changes in JGS of the kidneys were characterized by an increase in number of cells corresponding

to grades 3-4 granularity, while the JGI presented a statistically significant rise. It constituted 36.4±1.7 days after 3 h and 35.6±1.1 after 1 day (versus 28.1±1.2 in control rats). JGI did not differ appreciably from control levels on the 3d day of hypokinesia. On the 5th experimental day, we observed a maximum elevation of JGI (to 38.8±0.7). It declined thereafter. By the 10th day of hypokinesia JGI was negligibly above the control level, whereas on the 20th and 30th days we observed a decrease in both number of myoepithelioid cells, and in degree of granularity. The JGI dropped to 16.2±1.6 on the 20th day and to 22.3±0.9 on the 30th day.

Mean volumes of cortical and juxtamedullary glomerules of rat kidneys under hypokinetic conditions (n = 6)

Time	Glomerules					
	cortical			juxtamedullary		
	volume		P	volume		P
	thousands of μm^3	% of control		thousands of μm^3	% of control	
Intact rats	176.6±1.035	100.0±0.50		196.8±1.036	100.0±0.52	
After 3 h	167.5±1.077	96.0±0.61	0.001	220.3±0.934	110.8±0.47	0.001
1st day	158.4±1.144	89.7±0.65	0.001	206.2±0.974	103.7±0.50	0.001
3d "	203.6±0.90	115.3±0.51	0.001	242.9±0.855	122.2±0.43	0.001
5th "	145.2±1.254	82.2±0.71	0.001	206.6±0.994	103.9±0.50	0.001
10th "	169.0±1.077	95.7±0.61	0.001	181.7±1.131	91.4±0.57	0.001
20th "	159.4±1.148	89.7±0.65	0.001	194.4±1.054	97.8±0.53	0.02
30th "	156.3±1.166	88.5±0.66	0.001	172.8±1.191	86.9±0.60	0.001

Note: P refers to reliability of difference between experimental and control rats, with regard to glomerular volume.

It is apparent from the foregoing that there is a certain correlation between volume of cortical and juxtamedullary glomerules, on the one hand, and activity of JGS cells, on the other. The increase in functional activity of the JGS occurred during periods of redistribution of intrarenal blood flow, when there was morphological demonstration of cortical ischemia and plethora of juxtamedullary glomerules and cortical vessels. As we know, the phenomenon of shunting of renal blood occurs with various extreme factors and states [9, 14, 15], and it is one of the "defense reaction" effects [16].

It was established that cortical vasoconstriction is related not only to trarenal mechanisms, but is also considered as one of the variants of toregulation of renal blood flow, where the JGS occupies a special place]. The redistribution of intrarenal circulation between the cortical and juxtamedullary nephrons, which differ in capacity to reabsorb sodium [18], which occurs under hypokinetic conditions, may be one of the causes of the change in excretory function of the kidneys.

The decline of the JGI on the 20th and 30th days of hypokinesia corresponded in our experiments to a decrease in filling of cortical and juxtamedullary

glomerules. It is difficult to determine the cause-and-effect correlation between these changes, since the question of loc[a]lization of the vascular effect of renin in the kidneys has still not been answered. Moreover, the decline of JGI could occur due to decreased synthesis of renin or degranulation of myoepithelioid cells as a result of increased excretion thereof in blood plasma.

Activation of the renin-angiotensin system, which was observed at the early stages of the experiment, is consistent with the findings of other authors [19], and it was demonstrable during the period of increased functional activity of the adrenals. 11-HOC content of blood plasma increased to 14.83 μg% on the 3d day, versus 6.3 μg% in intact rats. Hyperadrenocorticism persisted on the 10th and 20th experimental days, although the mean 11-HOC levels at these times were lower (9.8±0.001 and 8.8±0.004 μg%, respectively).

It was shown that the nature of renal exretory function in response to administration of angiotensin depends on a number of conditions, including the animal species, its "steroid status," direction of related changes in glomerular filtration and renal blood flow [20]. It was previously reported [21] that administration of renin and angiotensin induces natriuresis and diuresis in rats (unlike man). This occurs as a reuslt of increase in the filtration fraction, decreased tubular reabsorption of sodium, attenuation of passive and active processes of reabsorption of fluid in the distal tubules. Depending on the secretion level, corticosteroids have a different influence on the effect of angiotensin. In the presence of states involving excessive corticosteroids there is enhancement of the effect of angiotensin [20]. Experiments involving administration of ACTH and hydrocortisone to rats demonstrated that this is associated with elevation of the renin substrate. In addition, adrenocortical hormones enhance pressor sensitivity to renin and angiotensin, which occurs as a result of a change in fluid-sodium balance and electrolyte composition of the vascular wall. The diuretic and natriuretic effects of glucocorticodes are also attributed to their antialdosterone effect in and outside the kidney, influence on renal hemodyanmics and the blocking of the ADH [antidiuretic hormone] effect [22]. The regulatory role of glucocorticoids in tubular permeability to fluids was demonstrated in experiments involving microperfusion of the tubules of healthy and adrenalectomized rats given glucocorticoids and mineralocorticoids [23]. In adrenalectomized rats, permeability of the wall of the distal tubules to fluid increased, and it reverted to normal only after giving them glucocorticoids. Thus, the submitted data show that the increases elimination of fluid and electrolytes observed in hypokinetic rats [3, 7] is due to activation of the renin-angiotensin system, the effect of whose hormones is apparently simulated by glucocorticoides. The latter circumstance, by virtue of antialdosterone effect and direct effect on filtration and tubular reabsorption, has a substantial influence on fluid-electrolyte metabolism under hypokinetic conditions.

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UDC: 61].17+612.35].015.32-06:612.766.2

EFFECT OF HYPOKINESIA ON CHANGES IN CARBOHYDRATE AND LIPID METABOLISM IN THE HEART AND LIVER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 57-62

[Article by Yu. P. Ryl'nikov, submitted 4 Apr 78]

[English abstract from source]

Rigid immobilization of rabbits is accompanied by a reduction of glycolysis rate in the liver and, particularly, in the heart and a simultaneous increase of the fraction of carbohydrate utilization in the pentose phosphate pathway. It is also followed by cholesterol accumulation in the blood and tissues in spite of an accelerated bile excretion of cholesterol and its derivatives — bile acids.

[Text] Inadequate physical activity increases the possibility of atherosclerosis and raises by 1.5-2 times the probability of myocardial infarction [1-3]. Experimental restriction of muscular activity is associated with changes in metabolic processes that are similar in nature to the changes observed with atherosclerosis [4-6]. The cholesterol and β-lipoprotein content of blood serum increases, and in tissues there is an increase in cholesterol with concurrent decrease in total lipids.

We have studied here the rate of assimilation of carbohydrates via glycolysis and the pentose-phosphate pathway, as well as changes in B bile in hypokinetic rabbits.

Methods

Experiments were conducted on 76 rabbits of both sexes weighing 2.5 to 3 kg. Control and experimental animals were kept on the usual feed diet. The experimental group of rabbits were kept in hypokinetic cages. We assayed glycogen [7], rate of glycolysis (according to difference between preformed lactate and increment thereof in 1 h of incubation in Krebs-Ringer buffer, pH 7.35 at 37°C with addition of 200 mg% glucose according to Barker and Summerson [8]) and activity of the pentose-phosphate pathway

(according to level of preformed pentoses and sedoheptuloses, and decline or elevation thereof when incubated with glucose or fructose-1,6-diphosphate [9]) in the liver and heart of the animals on the 10th, 15th, 30th and 60th experimental days. On the same days, we assayed B bile, cholesterol (according to Sperry and Brady as modified by P. Z. Khasigov [10]), bile acids (according to Shire-Kuhne as modified by N. P. Skakun [11]) and dry residue.

Results and Discussion

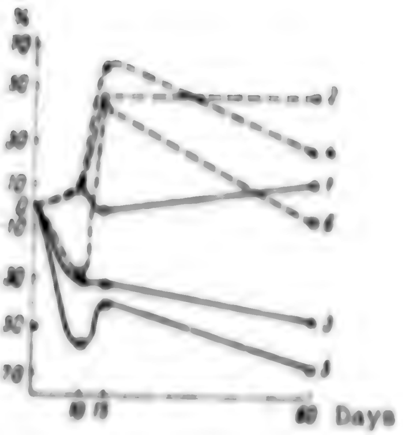
There was an appreciable decrease in liver glycogen content as a result of hypokinesia (by 64.12, 75.24, 81.68 and 82.81% after 10, 15, 30 and 60 days). Conversely, there was a reliable increase in glycogen content of the heart at the start of the experiment, followed by gradual decrease. By the 60th day, glycogen level in the heart was one-half the control level.

There was a tendency toward decrease in preformed lactate in the heart and liver (Table 1). Upon incubation of homogenates of these organs with glucose, lactate increment by the 10th day of hypokinesia was one-half the control level in the heart and remained at this level to the end of the study; in the liver it remained low to the 15th day.

Table 1. Changes in rate of glycolysis in tissues of hypokinetic rabbits

Duration of experiment, days	Number of animals	Statistical index	Lactate content, µmole/100 mg wet tissue			
			liver		heart	
			preformed	increment with incub. with glucose	preformed	increment with incub. with glucose
Control	7	M±m	0.82±0.05	0.79±0.02	2.64±0.06	2.16±0.04
10	6	M±m	0.54±0.12	0.40±0.04	2.16±0.34	1.03±0.41
		%	−34.15	−49.37	−18.18	−52.31
		P	>0.35	<0.01	>0.1	<0.02
15	5	M±m	0.55±0.04	0.52±0.06	2.52±0.18	1.50±0.18
		%	−32.93	−34.18	−4.35	−30.56
		P	<0.01	<0.01	>0.5	<0.01
30	5	M±m	0.62±0.08	0.71±0.10	1.86±0.14	0.78±0.17
		%	−24.39	−10.13	−29.55	−63.89
		P	>0.05	>0.4	<0.01	<0.01
60	5	M±m	0.70±0.08	0.66±0.15	2.80±0.20	1.15±0.12
		%	−14.63	−16.46	−6.06	−46.76
		P	>0.1	>0.4	>0.4	<0.01

There was a greater decrease in pentose content upon incubation of homogenates of the heart with glucose, as compared to the control (by 31.71, 32.78 and 49.05% after 10, 15 and 60 days, respectively), increase in sedoheptuloses (by 57.77% after 15 days and 23.19% after 60 days), with preservation of a constant level of preformed pentoses and sedoheptuloses



Levels of preformed pentoses (1) and sedoheptuloses (2) in heart tissue and changes therein upon incubation with glucose (3 and 4, respectively) and fructose-1,6-diphosphate (5 and 6) under hypokinetic conditions

(see Figure). When heart tissues were incubated with fructose-1,6-diphosphate, there was a more significant decrease in pentose content (by 57.17, 43.22 and 69.12% on the same days), but a reliable increase in sedoheptulose content (by 41.42%) was only noted after 2 weeks. Preformed pentose content of the liver remained constant. A tendency toward decrease therein was observed only by the end of the 2d experimental month (by 33.61%, P>0.05). When hepatic tissue was incubated with substrates the changes were also in the same direction: a tendency toward decrease in pentose content after 10 days (by 3.93%, as compared to glucose and by 13.13%, as compared to fructose-1,6-diphosphate), which was reliable by the end of the 2d week (by 13.24 and 15.20%, respectively). However, by the end of the experiment, the decrease in pentose content upon incubation of homogenates with substrates did not differ from the control. While preformed sedoheptuloses maintained a constant level, by the end of the experiment the increment thereof in the liver upon incubation with both substrates was the most significant (by 73.70% with glucose and 53.79% with fructose-1,6-diphosphate).

Thus, under hypokinetic conditions there was a decrease in rate of oxidation of glucose by means of glycolysis, with concurrent increase in share of assimilation via the pentose-phosphate pathway.

There was structural change in composition of B bile under hypokinetic conditions (Table 2).

During the first month of the experiment, we observed an increase in B bile content, with maximum increment after 2 weeks of limited mobility. At the same time, there was an increase in concentration of cholesterol in bile (by 2.5 times between the 10th and 30th days, and 1.5 times at the end of the experiment) and mean of 2-fold increase in bile acids throughout the experiment. There was also a reliable increase in amount of dry residue in the bile, as compared to the control.

Glycogen content of hepatic tissue diminished, apparently due to hyperproduction of catecholamines, the levels of which were significantly elevated in blood and urine at different stages of hypokinesia [6, 12-14]. The decrease in rate of glycolysis in liver and heart tissues is possibly

due to excessive accumulation of cholesterol in blood and tissues in the presence of hypokinesia [4-6, 15-18]. Excessive production of glucocorticoids under prolonged hypokinetic conditions [14] is also capable of depressing hexokinase activity [19].

Table 2. Changes in B bile parameters in hypokinetic rabbits

Duration of experiment, days	Statistical index	Bile, ml	Cholesterol mg%	Bile acids, mg%	Dry residue, %
Control	$M \pm m$	1,27 ± 0,24	255,67 ± 33,65	2311,09 ± 209,71	13,90 ± 1,04
	n	11	6	11	7
10	$M \pm m$	1,90 ± 0,46	871,60 ± 48,52	4712,40 ± 104,67	20,49 ± 1,91
	n	6	5	5	6
	%	+ 49,61	+ 240,91	+ 103,90	+ 47,41
	P	>0,2	<0,01	<0,01	<0,01
15	$M \pm m$	2,[illegible] ± 0,12	8[illegible],80 ± 100,0	5557,20 ± 853,31	21,05 ± 2,05
	n	5	5	5	5
	%	+ 126,77	+ 2[illegible],12	+ 140,46	+ 51,44
	P	<0,01	<0,01	<0,01	<0,02
30	$M \pm m$	1,72 ± 0,33	820,80 ± 106,87	[illegible],80 ± 800,54	23,37 ± 2,40
	n	5	5	5	5
	%	+ 35,43	+ 221,04	+ 145,12	+ 68,13
	P	>0,2	<0,01	<0,01	<0,01
60	$M \pm m$	1,23 ± 0,13	610,80 ± 55,[illegible]	5102,00 ± 733,47	20,62 ± 0,87
	n	6	5	5	6
	%	−3,15	+ 138,90	+ 120,76	+ 48,34
	P	<0,9	<0,01	<0,01	<0,01

The increased assimilation of carbohydrates via the pentose-phosphate pathway, which is observed under hypokinetic conditions, could occur both as a result of decline of Michaelis constant for glucose-6-phosphate dehydrogenase and due to activation of this enzyme by catecholamines [20-22], while 6-phosphogluconate is also an inhibitor of glycolysis [23]. Activation of the pentose pathway with dissociation of respiration and phosphorylation, which can occur during hypokinesia as a result of hyperproduction of epinephrine [12-14, 23, 24], enables the body to come out of the critical state by means of increase in reserve of $NADP \cdot H_2$ and ribose, which are needed for synthesis of lipids, nucleotides and nucleic acids. Activation of the pentose pathway in the heart makes it possible for cells of the contractile myocardium to recover as a result of mitochondrial hyperplasia [25].

The excessive production of epinephrine under hypokinetic conditions [12-14] causes changes in the myocardium [4, 26] and activation of lipolysis. However, the associated decrease in activity of citrate synthetase and acetoacetyl-CoA-thiolase [27], as well as inadequate oxygen uptake [15, 24], could cause accumulation in the body of products of incomplete oxidation

of fatty acids [28]. The excessively accumulated acetone bodies are apparently not only eliminated, but utilized for synthesis of cholesterol and fatty acids, which is added by replenishment in tissues of NADP·H$_2$ reserves as a result of activation of the pentose pathway. There is progressive increase in blood and tissular β-lipoprotein content with increase in duration of hypokinesia [4-6, 15, 16], which indirectly favors the above hypothesis. The elevation of levels of 6-phosphogluconate and transport forms of cholesterol decreases the activity of enzymes of the glycolytic pathway, closing the circle of changes in metabolic processes in the presence of "rigid" hypokinesia.

In an effort to get rid of excessive cholesterol, the body eliminates it in bile and there is more active transformation into bile acids (see Table 2). Activation of this process conforms with maximum increase in blood cholesterol [6, 15, 16], and it is observed 2-3 weeks after the start of hypokinesia. The progressive hyper-β-lipoproteinemia associated with restricted movement is the factor that stimulates bile production, since synthesis of bile acids is possible only at the expense of β-lipoprotein cholesterol [29]. The increased transformation of cholesterol into bile acids, as well as intensified elimination thereof in bile, are adaptive reactions of the body that permit it to partially rid itself of excessive amounts thereof. On the first days of restricted movement, part of the cholesterol is apparently converted into corticosteroids, since the levels thereof in blood increase [5]. However, synthesis of corticosteroids and sex hormones from cholesterol can only occur when there is adequate activity of the tricarboxylic acid cycle, since oxidation of the side chain of cholesterol for production of progesterone requires adequate amounts of pyruvate, malate and NADP [30]. In the case of prolonged hypokinesia, utilization of cholesterol for synthesis of sex hormones and corticosteroids apparently diminishes, due to decreased activity of Krebs' cycle [27].

When there was inadequate physical activity, there was an increase in cholesterol content of the heart and, particularly, the liver, which was more significant in old animals, in spite of the above-mentioned defense mechanisms [6, 15]. We were impressed by the close correlation between levels of cholesterol in blood, tissues and bile (see Figure). The decreased elimination of cholesterol in bile toward the end of the 2d month of hypokinesia was associated with concurrent elevation of its level in blood and the liver.

Consequently, under hypokinetic conditions the fatty acids from the pool, as well as those synthesized de novo, undergoing partial oxidation, replenish the reserve of acetone bodies, which are either eliminated from the body or utilized again for synthesis of fatty acids and cholesterol. Cholesterol is metabolically less active, and for this reason the level thereof gradually rises in blood and tissues under hypokinetic conditions.

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UDC: 612.633-06:612.273.2.017.2

EFFECT OF CONDITIONING FOR HYPOXIA ON FERTILITY OF WHITE MICE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 62-66

[Article by V. B. Malkin and Ye. A. Stroganova, submitted 7 Apr 78]

[English abstract from source]

The purpose of the study was to investigate a prolonged effect of hypoxia on the reproductive function and development of pups of white mice. Beginning with the age of 2 months the animals were exposed to an altitude of 7500 m for 6 hours a day during 9 months. The mice that were so adapted to and mated in hypoxia did not deliver any offspring. The animals that were adapted to hypoxia during intrauterine and postnatal development and mated at 5500 m delivered normal although much smaller litters.

[Text] Some researchers propose the use of an artificial gas environment with low partial oxygen pressure in the pressurized cabins of spacecraft to prevent asthenization of cosmonauts during long-term flights. This suggestion is based on the fact that adaptation to hypoxia has a stimulating effect on hemopoiesis, respiratory function and circulation.

A comparative evaluation of different conditioning regimens revealed that intermittent exposure to hypoxia (6-7 h/day) has a more marked conditioning effect than continuous exposure to the same altitude [1]. In view of the foregoing, there is reason to assume that with the use of an "active" hypoxic atmosphere one can select modes with which the cosmonauts would be exposed daily for several hours to the effects of insufficient oxygen in the inhaled air. This makes it necessary to pursue a comprehensive study of the effects of such conditioning not only on the functional state of the body, but such important biological parameters as reproductive capacity, mean life expectancy and others.

There is information in the literature to the effect that prolonged shortage of oxygen in inhaled air leads to depression of reproductive function [2, 3].

Experimental studies of the effects of hypoxia on animal fertility established that with increase in altitude to which the animals were exposed

there was a decrease in fertility [1, 3, 4]. Evidently, both neuroendocrine changes in the female, as a result of which there is impairment of the mechanism of normal implantation of a fertilized ovum in the uterine wall [5], and the direct deleterious effect of hypoxia on the process of spermatogenesis, maturation of follicles and, perhaps, the embyro itself [6] are the causes of this decrease in fertility.

Our objective here was to study the effect of a prolonged shortage of oxygen in the gas environment on reproductive function of white mice and development of offspring.

Methods

Experiments were conducted on mongrel white mice at the age of 2 months. The study lasted 9 months. At the first stage of the experiment, all of the animals, with the exception of a control group, were adapted to hypoxia in a pressure chamber. Conditioning lasted 30 days, during which the animals were raised daily to increasing altitudes (from 3000 to 5500 m). They remained at each level for 6 h/day. Thereafter, to maintain the conditioning effect, the animals were divided into four groups. Each group consisted of 6-9 females and 3 males kept separately. The first group was exposed to an "altitude" of 5500 m for 6 h daily, with the exception of Sundays; the second was conditioned once a week ("altitude" of 5500 m for 6 h); the third was conditioned twice a week on the same schedule. The fourth group (control) was kept in the vivarium throughout the experiment. On the 56th day of the experiment, the males and females of all groups were put together for 15 days for mating, and conditioning on the same program continued in the pressure chamber. The animals were weighed before mating. In addition, we singled out a group of females that was put together with males for 5 h twice a week only at an "altitude" of 5500 m (altitude group). The general condition of animals in all groups was satisfactory after 2 months of the experiment, prior to mating. The mean weight of males constituted 25.5, 25, 27 and 31 g in the 1st, 2d, 3d and 4th groups, respectively; the mean weight of females constituted 23.6, 23.5, 26.3 and 25 g, respectively. In the altitude group, mean weight of males was 28 g and that of females was 26 g.

Results and Discussion

In the 1st-3d groups, whelping began at the same time, on the 21st-22d day. It started several days later in the 4th group, but occurred within 2 days, whereas in the first 3 groups it extended over 6-7 days.

In the 1st group, 3 out of 7 females dropped pups. The mean number of offpsring per female constituted 6.6. In the 2d group, 5 out of 7 females had offspring. There were 6.4 mice per female. In the 3d group, 8 out of 9 females gave birth. The mean number of offspring per female was 5.7. In the 4th group, 4 out of 6 females had offspring, with a mean of 5 mice per

litter. Thus, whelping was at a lower level in the first group, which was submitted to the most intensive (daily) conditioning in the pressure chamber, than in the other groups.

Table 1. Reproductive capacity of mice in different groups and characteristics of their offspring

Index	Animal group							
	1		2		3		4	
	offspring (litter)							
	first	second	first	second	1st	2d	1st	2d
Whelping, day after putting male with female	22—29	23—24	22—28	21—25	21—27	21—30	25—26	24—26
Mean number of offspring per female	6.6	6.6	6,4	8.6	5.7	7.2	5	8
P	<0.01	<0.01	<0.01	>0.05	>0.05	>0.05	—	—
Mean weight of 1-day-old mice, g	—	1.4	—	1.3	—	1.7	—	1.5
P	—	>0.05	—	>0.05	—	>0.05	—	—
Mean wt. of 10-day-old mice, g	4.4	5.0	4,9	3.7	5.7	5.2	7.5	4.8
P	<0.01	>0.05	<0,01	>0.05	<0.01	>0.05	—	—
Mean wt. of 20-day-old mice, g	7.9	7.6	7.4	7.5	7.6	8.7	9,2	10,0
P	>0,05	<0.01	<0,01	<0,01	>0.05	>0.05	—	—
Mean wt. of 30-day-old mice, g	12,1	9.3	11,8	11.5	13,6	12.9	15,8	15,4
P	<0.05	<0,01	<0.01	<0.01	>0.05	>0.05	—	—

Note: Exposure to hypoxia before mating of the 1st, 2d and 3d groups lasted 55 days in obtaining the first litters of offspring and 138 days for the second litters.

As can be seen in Table 1, the mean number of mice per litter in the 1st and 2d groups was higher than in the 1st (control) group by 1.6 and 1.4, respectively. The results are statistically reliable (P<0.01). In the "altitude" group, only 1 out of 6 females had offspring on the 25th day. The litter consisted of one stillborn mouse. Thus, when males and females were mated only at an "altitude" of 5500 m there was a drastic decrease in reproduction (in fact, it was almost entirely suppressed). In the subsequent course of the experiment, we continued to condition the parents, together with the offspring, in the pressure chamber. We monitored development of the offspring from the time of birth. As shown in Table 1, the mice delivered by the 1st group of animals weighed an average of 2.7, 1.3 and 3.7 g less than in the control on the 10th, 20th and 30th days,

respectively. These differences in weight were statistically reliable ($P<0.005$, $P<0.01$). The mean weight of offspring delivered by the second group of animals was 2.6, 1.8 and 4 g lower than in the control at the age of 10, 20 and 30 days, respectively. The results were statistically reliable ($P<0.01$). The mean weight of mice delivered by the 3d group was lower than in the control; however, these differences were statistically reliable only at the age of 10 days ($P<0.01$).

Fur growth began almost simultaneously in all groups. After 30 days, the offspring were separated from the parents and, like before, all of the animals (offspring and parents) continued to be conditioned to an "altitude" of 5500 m. At the age of 6.5 months, the parents were again put together for mating. Second litters were obtained in all groups. The mean weight of the offspring at birth was virtually the same in all 4 groups, ranging from 1.3 to 1.7 g. In the next 10 days, weight gain was uniform in offspring of the 1st, 3d and 4th groups. Only in the 2d group was there a tendency toward 1.4-g decrease in mean weight, as compared to the control. At the age of 20 days, the mean weight of mice in the 1st-3d groups was 2.4, 2.5 and 1.3 g less than in the control. The results were statistically reliable ($P<0.01$) in the 1st and 2d groups. At the age of 30 days, the mean weight of offspring in the 1st-3d groups was 6.1, 3.9 and 2.5 g less, respectively, than in the control. The difference was statistically reliable in the 1st group ($P<0.01$).

It was very interesting to see if offspring would be obtained from animals that had been exposed to hypoxia in the intrauterine period. For this purpose, we took mice from the first litters born to animals on the 7[illegible]h-80th day of the experiment. At mating time these animals had reached the age of 4 months. By this time, the mean weight of males in the 1st-4th groups constituted 30, 30, 27 and 38 g, respectively, and that of females 22.8, 25.5, 25 and 35.3 g. In the "altitude" group, the mean weight of males was 30 g and females 35.3 g.

All groups of experimental animals produced offspring. Thus, it may be considered that animals preconditioned to hypoxia reproduced on virtually the normal (control) level. As can be seen in Table 2, in all three groups there were fewer mice per female that gave birth than in the 4th (control) group: by a mean of 1.9, 4.1 and 2.5, respectively. The differences were statistically reliable ($P<0.01$). In the "altitude" group, 2 out of 5 mice produced offspring. There was a mean of 5.5 mice per litter.

The mean weight of offspring at the age of 1 day was virtually the same in all groups. As shown in Table 2, weight gain for the next 10 days was uniform in all groups. However, at the age of 20 and 30 days, there was a lag in weight gain of animals in the 1st and 3d groups. Weight gain in animals born to the "altitude" group of parents was close to the control level. Interestingly enough, normal offspring was delivered by animals of the "altitude" group, which had been exposed to hypoxia from the time of birth, whereas no offspring had been obtained from their parents, i.e.,

animals first used in the experiment at the age of 2 months and put in the "altitude" group, in spite of the fact that these mice were of the same age. The increase in number of mice per second litter from parents weighing less can apparently be attributed to the fact that the females usually deliver considerably smaller offspring the first time. The offspring delivered by animals exposed to a shortage of oxygen in the pressure chamber during embryogenesis differed substantially in number from the control group. There were 1.9, 4.1 and 2.5 fewer mice per litter than in the control in the 1st-3d groups, respectively. The differences were statistically reliable. Reproduction was close to the control in females that were conditioned from the time of birth. Thus, reproductive capacity was somewhat higher in animals submitted to hypoxic conditioning while still in the intrauterine stage of development and periodically exposed from the time of birth to a gas environment markedly deficient in oxygen, i.e., animals adapted to the prolonged effect of hypoxia, than in mice exposed to hypoxia for the first time at the age of 2 months.

Table 2. Reproductive capacity of mice in different groups and characteristics of their offspring (third litters)

Index	Animal group				
	1	2	3	4	"altitude"
Exposure to hypoxia prior to mating, months	4	4	4		4
Day of whelping, from time male was put with female	20—23	20—28	20—23	20—26	19—25
Mean number of offspring per whelping female	7.2	5	6.6	9.1	5.5
P	<0.01	<0.01	<0.01	—	—
Mean wt. of day-old mouse, g	1.4	1.8	1.5	1.4	1.6
P	>0.05	>0.05	>0.05	—	—
Mean wt. of 10-day-old mouse, g	4.4	5.7	4.7	5.2	4.5
P	<0.05	>0.05	>0.05	—	—
Mean wt. of 20-day-old mouse, g	6.04	8.7	7.2	8	9
P	<0.01	>0.05	>0.05	—	—
Mean wt. of 30-day-old mouse, g	11.7	13.3	12.3	14.7	15.0
P	<0.01	>0.01	<0.01	—	—

As a result of this study, it was established that daily exposure of animals to oxygen-deficient conditions corresponding to an "altitude of 5500 m for 6 h/day did not prevent reproduction, unlike other conditioning programs.

Under the hypoxic conditioning schedule that we selected, the offspring developed normally, and there was only some lag in weight gain of newborn animals submitted to conditioning.

The above data and results of a previous study [1] are indicative of the desirability of using "split" programs of conditioning to hypoxia, i.e., a schedule that involves daily alternation of exposure to a shortage of oxygen and normal conditions.

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UDC: 612.392.99

THE QUESTION OF USING DEHYDRATED FOODS DURING LONG-TERM SPACE FLIGHTS

Moscow KOSMICHESKAYA B O OGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 66-70

[Article by V. P. Bychkov and V. Markaryan, submitted 3 Apr 78]

[English abstract from source]

The paper discusses the results of five studies on 35 test subjects conducted to test diets of dehydrated products to be used in prolonged space flights. The studies have demonstrated that a diet consisting of only dehydrated food products can be used for a prolonged time (up to 1 year). Dehydrated foods after a 2-year storage and proton irradiation at a dose of 24,000 rad retain their biological value and assure an adequate nutritional status. On this basis a space diet composed of dehydrated foods has been developed

[Text] Before reliable and economical methods are developed for producing food for long-term space flights, apparently the crew will consume primarily dehydrated products [1, 2].

Development of food rations consisting of dehydrated foodstuffs for long-term space flights requires determination of the possibility of long-term intake of dehydrated foods under ordinary living conditions and in a pressure chamber, as well as studies of the influence of storage time and possible levels and spectrum of radiation during long-term (up to 2 years) space flights on biological value of foods, determination of forms and assortment of dehydrated foods suitable to make up food rations for long-term space flights. We submit the results of these studies in this report.

Methods

We conducted 5 studies with the participation of 35 volunteer subjects ranging in age from 19 to 49 years. In the first study, 6 subjects were on a diet for 120 days consisting entirely of dehydrated foods, under customary living conditions. In the second study, 3 subjects received

the same rations, but in a pressure chamber with an artificial habitat. For 1 month before and after the study, their diet consisted of freshly prepared foods analogous in chemical composition to the experimental ration. In the third and fourth series of studies, the dehydrated products had been stored for 2 years previously, and some were exposed to divided doses of proton radiation totaling 24,000 rad (6000 rad every 6 months). The radiation dose for the foods was determined on the basis of analysis of the radiation situation during long-term space flights over a period of several years, when the cumulative dose, referable chiefly to protons from solar bursts, could constitute tens of thousands of rad with shielding about 1 g/cm^2 in thickness [3]. The technique for irradiation was described previously [4]. In the third study, 5 subjects consumed dehydrated products, after storage for 1 year and exposure to 12,000 rad, for 70 days; concurrenlty 5 other subjects consumed the same foods, but they were not exposed to radiation. The fourth study involved 10 subjects and an analogous program, but with the use of foods after storage for 2 years and exposure to radiation in a dose of 24,000 rad. In the fifth study, 6 subjects consumed for 60 days dehydrated foods which, according to the results of the preceding studies, were recommended for rations for long-term space flights. In the last three studies, the subjects spent their free time in a specially reserved room under observation by medical personnel. Table 1 lists the characteristics of the diets. The diets were analyzed for levels of main nutrients and minerals. Each day, the subjects took 1 Undevit multiple vitamin lozenge. Fluid intake was not restricted, but a strict record thereof was kept.

Table 1. Nutrients contained in food rations (analytical data)

Study No.	Protein g/day	Fats g/day	Carbo-hydrates g/day	Calories, kcal/day
1	128	96	411	3100
2	131	125	344	3110
3	140	96	420	3200
4	140	96	420	3200
5	143	100	430	3280

The foods were dehydrated mainly by the freeze-dry method [5]. Some foods were dehydrated by heat drying. Development of the rations was made with the immediate participation of the All-Union Scientific Research Institute of the Food Canning and Vegetable Drying Industry under the USSR Ministry of the Food Industry. The subjects were under medical supervision, which involved physical examination, weighing, checking the pulse, body temperature and blood pressure. Peripheral blood was submitted to clinical analysis once every 10 days. Throughout the period of these

studies the subjects rated the dishes and products on a 5-point scale. We examined the parameters characterizing protein, lipid, carbohydrate, vitamin, fluid-mineral metabolism, functional state of the adrenals and liver; we determined assimilation of the main nutrients and balance of a number of elements; we tested immunological reactivity of the body and composition of intestinal microflora. The results were submitted to processing by the method of variational statistics.

Results and Discussion

Throughout the 1st and 2d studies, the general well-being of the subjects was satisfactory. Pulse rate and arterial pressure did not exceed the range of physiological fluctuations. We failed to demonstrate pathological changes in morphology of peripheral blood. Weight loss was observed only in subjects who were significantly overweight with an initial weight of more than 75 kg.

In the 1st study, we found increase in general acidity and free hydrochloric acid in gastric juice. Subjectively, 4 out of 6 subjects reported varying degrees of heartburn for the first 2 months of the test. At the end of the 3d month, acidity of gastric juice began to diminish, and it returned almost to the base level by the end of the 4th month. These changes can be attributed to the process of adaptation of the digestive system to dehydrated foods [6]. In the 2d study, there was also a change in acidity of gastric juice, but it was inconsistent.

Total protein content of blood serum was in the normal range in both studies, and it differed insignificantly at different stages (7.5 to 8.1 g% in the first and 7.34 to 8.3 g% in the second). Electrophoregrams revealed an increase in albumin fraction in the 2d and 3d months of the first study ($P<0.05$). Concurrently there was a decrease in globulin concentration referable to the α- and β-fractions. By the 4th month of intake of the experimental ration, the levels of these fractions reverted to the background values [7]. There were insignificant changes in the blood serum proteinogram of subjects in the second study, and they did not exceed the range of physiological fluctuations. The similarity of results, indicative of absence of decrease in blood serum albumin fraction in both studies, enabled us to conclude that there was adequate protein intake, both qualitatively and quantitatively, on the experimental diets [8, 9].

In the first study, there was a decrease in concentration of most free amino acids of blood serum for the first 2-3 months of the period tested. The most marked decline was referable to glutamic acid, threonine, methionine and valine ($P<0.001$). In the 4th month, there was an increase in concentration of essential and nonessential amino acids. Evidently, the decline in level of free amino acids occurred as a result of poorer digestibility of proteins in dehydrated products by the proteolytic enzymes of the gastrointestinal tract. In the second study, we observed a decline of blood serum levels of some amino acids in different months.

Comparative analysis of the results of examining the end products of nitrogen metabolism revealed that excretion of total nitrogen, uric acid and creatinine in 24-h urine was at about the same level and within the physiological range in subjects participating in the first and second studies, whereas the nitrogen balance was close to zero or positive. These data are also indicative of the fact that the diets were satisfactory in protein content.

We failed to demonstrate appreciable changes in lipid metabolism (total lipids, α- and β-lipoproteins, total, esterified and free cholesterol) and vitamin metabolism (B_1, B_2, C, A, E and carotene). Blood sugar levels were in the physiological range [10] in both studies; fluid metabolism constituted 3005 ml in the first study and 2727 mℓ in the second, i.e., there was an average of about 1 mℓ fluid per kcal energy consumed. In the first study, we failed to demonstrate significant changes in balance of the main biogenous elements (N, P, Mg, S, K, Na, Cl), with the exception of Ca in the 3d and 4th months of the experimental period due to significant decrease in assimilation. In the second study, Ca content of the diet was increased from 0.82 to 1.27 g/day. The amount of minerals in the diet of subjects involved in the second study, including Ca, was sufficient to maintain the balance thereof in the body.

Assimilation of main nutrients from dehydrated foods was not lower than from analogous freshly prepared foodstuffs (Table 2).

Table 2. Assimilation of main nutrients in the diets, %

Nutrients	Study No								
	1		2		3		4		5
	diets								
	background	experimental	background	experimental	after 1-yr storage	after 1-yr storage and 12,000 rad radiation	after 2-yr storage	after 2-yr storage and 24,000 rad radiation	experimental
Proteins	88.6	88.3	90.0	90.6	88.0	86.0	87.0	89.0	90.0
Fats	93.4	96.6	95.1	97.5	96.4	96.8	97.0	97.0	97.0
Carbohydrates	96.1	95.0	98.0	96.6	97.8	97.4	96.0	96.0	97.0

The results of these studies enabled us to conclude that it is possible for man to stay on a diet consisting entirely of dehydrated foods for a long period of time (up to 1 year) [11].

Since radiation induces a number of changes in chemical composition of foods [12, 13], it was necessary to determine how the doses, spectrum

of radiation and prolonged storage expected during a space flight would affect the biological value of dehydrated foods.

At first, we studied the biological value of the diet of rats exposed to γ-rays and protons in a dosage of 70,000 rad. It was shown that after being given the experimental diet for 6-7 months there were no appreciable changes in weight of the animals, weight of internal organs, peripheral blood, amino acid composition of blood serum, total protein and protein fractions, as well as levels of sugar, cholesterol, total lipids, lipoproteins vitamins E and B group in the rats' blood [14].

As a result of the third and fourth studies, it was established that most of the tested dehydrated foods retained their biological value, according to organoleptic, physicochemical, biochemical and bacteriological tests, and provided for a satisfactory nutritional status of the subjects after storage of food for 1 year and exposure to protons in a dosage of 12,000 rad, as well as after 2-year storage and exposure to up to 24,000 rad. The data in Table 2 are indicative of a high degree of assimilation of the diets of freshly prepared dehydrated foods [15]. Examination of gastric juice after termination of the studies of subjects with diminished gastric secretion revealed an increase to normal levels, whereas in subjects with normal and somewhat elevated gastric secretion the parameters remained in the range of initial values.

All of the foodstuffs and dishes contained in the experimental diets were entirely consumed by the subjects. The mean rating thereof was 4. As a result of these studies, determination was made of the list of dehydrated foods and dishes that were suitable for making up a diet, the adequacy of which with regard to plastic and energy requirements of man was tested in the fifth study.

At the first stage of this study, there was a tendency toward decrease in free amino acid content of blood plasma and a statistically reliable increase in amino nitrogen of urine ($P<0.01$). As in the first study, it may be assumed that there was retention of release and absorption of some amino acid due to the poorer digestibility of proteins in dehydrated foods by digestive system enzymes. As we know, an amino acid imbalance diminishes utilization of amino acids for protein synthesis, and it is associated with increased excretion of amino acids in urine [16].

Total protein content of blood serum, particularly albumins, diminished ($P<0.05$); this also applied to hemoglobin; these are the "mobile" protein reserves of the body, which diminish when there is insufficient delivery of amino aicds to tissues [9]. By the 45th day of the study, all of these parameters reverted to background levels, and this can be interpreted as adjustment of the subjects to the altered diet.

For 60 days, the experimental diet provided for a normal health status, good level of performance by the subjects; it did not induce appreciable

changes in lipid, carbohydrate, fluid-mineral and vitamin metabolism. The parameters characterizing immunological reactivity of the subjects were also quite stable. The composition of a diet consisting of dehydrated foods for use during long-term space flights was defined and recommended on the basis of the results of these studies.

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UDC: 614.3:629.78-03

SYSTEM OF HYGIENIC INSPECTION OF NONMETAL MATERIALS USED IN SPACECRAFT EQUIPMENT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 70-74

[Article by G. I. Solomin, submitted 3 May 78]

[English abstract from source]

In view of a wide use of polymers in the spacecraft interior and their potential hazard, a system of hygienic control over their safety at every manufacture stage has been introduced. The system includes an analysis of a list of polymers, laboratory testing of samples under standard conditions; bench testing of various polymers used in the hardware and software under operational conditions; an examination of space cabin environments in real flights. The system of hygienic control allows selection of the safest polymers, i. e. those with minimum outgasing.

[Text] The conditions under which polymers are used in spacecraft differ significantly from all others, and they could affect the level of outgasing and, consequently, their toxicity [1-3]. For this reason, one of the pressing tasks is to study the long-term effect on materials of the main microclimate factors in a pressurized space: high temperature, humidity, air flow velocity, altered gas composition and low barometric pressure. In addition, at temperatures that are below those at which polymers are destroyed, there may be a linear dependence of outgasing on temperature level. At the time the destruction temperature is reached there is a sharp increase in outgasing, and this may be associated not only with a change in amount of released substances but a change in their composition. Lowering of barometric pressure to 258 mm Hg with concurrent change in gas composition of the environment in a sealed space lead to 3-4-fold increase in concentrations of chemicals. An increase in air humidity is also usually associated with an increase in concentration of volatile products in the gas phase. An increase in linear velocity of air above the polymer has a significant influence on the outgasing process. A higher level of trace impurities was found when the velocity of air above a polymer was increased to 0.15-0.20 m/s. Further increase in air velocity

did not affect the rate of outgasing which was determined only by the process of diffusion of low molecular substances in the polymer [4].

It was established th t there is a proportionate dependence of outgasing on saturation for a number of porous, film materials, rubbers and adhesives. In the case of long-term storage of polymer samples in a sealed space (up to 7 months), there is an exponential decrease in discharge of chemicals [5].

All of the foregoing prompted development and scientific substantiation of a system of hygienic control for the safe use of nonmetal materials used in the equipment of manned pressurized cabins of spacecraft. The system of hygienic inspection [control] that exists at the present time involves the following: screening of materials that do not release volatile products or present minimal outgasing when exposed to a temperature of 40°C; sanitary-chemical and toxicological testing of outgasing products from materials that were previously not examined in the laboratory and about the safety of which there is no information; development of steps to diminish outgasing (methods of hygienic "refinement"); development of recommendations pertaining to creation of heat-stable materials by improving the technology of their production, search for nontoxic raw material and additives; investigation of products of outgasing in the air environment of pressurized compartments.

Hygienic inspections are performed in the following manner, in accordance with the stages in construction of spacecraft:

1) primary analysis of the list of nonmetal materials used in a given item; 2) laboratory testing of each sample individually under standard conditions (saturation 1 kg, 1 g, 1 m^2, 1 pm per m^3 volume; temperature 40°C; barometric pressure 760 mm Hg; relative humidity 60-70%) or with specified parameters of the environment; 3) bench testing of different groups of materials under specified operating conditions; 4) mockup testing of the entire aggregate of nonmetal materials used under conditions that are as close as possible to real ones; 5) identification of products of polymer outgasing and quantitative assay thereof in the air of manned compartments of spacecraft in the course of flights.

The objective of hygienic analysis of the list of nonmetal materials is to screen samples for further investigation at the stage of laboratory testing, as well as to determine the entire scope of subsequent studies with due consideration of the target date for construction of the unit. Materials having no toxicological significance (wood, paper, etc.), as well as polymers contaning substances referable to the class of extremely toxic compounds (overt allergens, carcinogens, mutagens, etc.) are not submitted to study at the laboratory test stage. The latter materials are generally banned from use in pressurized compartments. Moreover, in the case of low saturation of a material (up to 100 cm^2/m^3 or less than 1.0 g/m^3) and low operating temperature (up to 40°C), the question of

necessity for sanitary and chemical tests can be settled on the basis of certificate data concerning the composition of polymer material and technology of its manufacture. When examining the list of materials, such indices as presence of GOST or technical conditions are taken into consideration. Use of experimental samples is permitted in exceptional cases and then only after they have been submitted to the complete schedule of examination.

At the second stage of hygienic control, experimental sanitary-chemical and, when necessary, toxicological studies of each sample individually are made. In view of the fact that there is a rather large volume of work at this stage, use of high-speed express methods for testing materials is justified [6, 7]. Hygienic evaluation on the basis of the results of sanitary chemical analysis is made by comparing outgasing levels referable to the different chemicals to their maximum permissible concentrations (MPC) in the air of sealed compartments. Due consideration is given to the nature of the expected combined effect by means of demonstration of substantces that have effects in the same direction. In those cases when a material discharges several toxic substances with the same direction of action, each of which is at the level or below the relevant MPC, determination is made of the overall index of the demonstrated concentrations in relation to their MPC. If the overall index does not exceed or equals 1, the material can be given a preliminary positive rating [8].

Studies of more than 500 polymer materials in the laboratory revealed that about 100 names of chemicals were identified in the process of gas chromatographic analysis of the products of outgasing of various polymers [9]. As a result of the studies, it was established that chemical compounds referable to saturated, unsaturated and aromatic hydrocarbons, aldehydes and alcohols are encountered the most frequently in the gas complex. Paints, varnishes and enamels emit the most gases (up to 80%). The levels of demonstrated concentrations most often constitute 0.9-0.01 mg/m^3. However, equiponderant concentrations of different components may constitute up to tens of milligrams per m^3. Toxicologically, the gas complexes should be considered as a low intensity factor.

Thus, the objective of work done at the stage of laboratory testing is to screen samples of materials with the lowest outgasing level, i.e., to obtain data concerning their relative toxicity.

At the stage of laboratory testing, odorimetric tests are also performed if necessary. Materials with a distinct odor are not recommended, since we know that substances capable of stimulating the receptors of the nose and upper respiratory tract induce, in addition to a sensation of odor or irritation, several undesirable reflex reactions, which alter the rate and amplitude of respiratory excursions, tonus of blood vessels, induce nausea, etc.

The bench tests are conducted on different groups of materials which are most often components of diverse equipment and instruments. In these tests it is possible to reproduce and maintain for a long time any specific operating conditions. Reproduction of specified conditions makes it possible to obtain the most objective information about the nature of emission of volatile substances, as well as to determine the degree of their possible effects on animals and man.

Numerous studies at the bench test stage revealed that the levels of chemicals emitted by a group of materials do not reach the levels of overall concentrations of the same substances demonstrated in the laboratory for individual polymers. This phenomenon is attributable to a number of factors, and in particular to the "shielding effect," which arises because of the reciprocal location of polymers in products and equipment. The reciprocal influence of materials on the outgasing process is manifested by a significant decrease in concentrations of the different products discharged by each of the tested samples individually, while a number of components are not demonstrable at all in such cases [10]. Moreover, it was established that some of the water-soluble compounds migrate into the condensate of atmospheric humidity [11].

A special device was developed for toxicological studies of the possible deleterious effects of polymer outgasing products, and it permits testing in a closed space [2]. When examining the functional state of animals, use is made of both integral indices characterizing the gas complex as a whole and specific tests for demonstration of the toxic effects of the main components, as well as functional load methods which make greater demands of the organism.

The fourth stage of examination of materials involves a number of mockup tests, including some with the participation of man, where the entire aggregate of polymers is used that had undergone prior examination under conditions that were as close as possible to actual ones. These tests include examination of air in the mockup with the use of heat tests. Here, determination is made of pollution of the air environment of manned pressurized compartments by polymers. It is important and mandatory to test the life support systems; in the course of these tests studies are made of the efficacy of regular [standard] systems of air purification, as well as complex medical studies of the air environment as a whole with due consideration of human gas emission. In the mockup tests, a complex evaluation is made of polymers, including other expected effects: presence and level of static electricity, biostability of polymers, dust content of air, etc. The results of the mockup tests revealed that the number of trace impurities discharged by polymers is up to 20-30. Many of them are the products of human gas emission. The volatile products include saturated, unsaturated and aromatic hydrocarbons, aldehydes, ammonia, carbon monoxide, acetates, alcohols, acetone, organochlorine compounds in concentrations at levels that are permissible for the air of pressurized compartments.

In conclusion, it must be noted that introduction of a scientifically substantiated system of hygienic supervision of safe use of polymers made it possible to lower significantly the level of outgasing in manned compartments of spacecraft. At the same time, experience in hygienic rating of materials shows that, with the every increasing duration of space flights, one should expand comprehensively the work pertaining to screening of the best materials, from the toxicological point of view, as well as development of stable, heat-resistant polymers. It is also imperative to try to limit the use of a wide diversity of synthetic materials, to standardize them, to make more use of methods of preliminary "refinement" of polymers that discharge toxic impurities and, at the same time, to search for methods of effective purification of the air in pressurized compartments.

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UDC: 582.264.45-155:572.5/.9:574.682

STUDY OF COMPATIBILITY OF CERTAIN HIGHER PLANTS AND CHLORELLA AS RELATED TO A BIOREGENERATIVE HUMAN LIFE SUPPORT SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 74-78

[Article by Yu. I. Shaydorov, B. N. Shebalin and G. I. Melesnko, submitted 15 May 78]

[English abstract from source]

The phototrophic component of a bioregenerative life support system should be of a multispecies structure. It should incorporate not only higher plants but also different algae. The paper discusses the studies concerning mutual effects of Chlorella and higher plants cultivated together in a closed atmosphere. It can be inferred from the studies that gaseous products of Chlorella did not exert a significant effect on the carbon dioxide consumption by wheat and radish plants or on their biomass increment. In turn, gaseous products of higher plants did not influence Chlorella growth. It can, therefore, be concluded that Chlorella and the above higher plants, when cultivated in a common atmosphere, do not inhibit each other and can be regarded as biologically compatible constituents of the photoautotrophic component of future bioregenerative life support systems.

[Text] The photoautotrophic elements of future bioregenerative life support systems should have a multispecific structure. According to the established opinion, the photoautotrophic element should include, along with higher plants, various forms of unicellular algae. The unquestionable superiority of higher plants from the standpoint of nutrition would thus be combined with the high technological effectiveness and controllability of unicellular algae [1].

The great stability of natural biocenoses is indicative of the presence in them of informative-controlling relations between the forms of organisms of which they consist. One of the mechanisms of such connections is the direct link via metabolic products released into the common environment they inhabit. Investigation of the reciprocal influence by means of released metabolites is a mandatory prerequisite for developing closed bioregenerative human life support systems, in which the direct correlations between components are known to be more marked than under ordinary conditions, because of the restricted space and specific amount of inert environment.

Cultivation of higher plants and chlorella in a human life support system that was closed for gas exchange did not yield an unequivocal answer to the question of compatibility of the components studied [2].

At the same time, microalgae and higher plants can be classified in groups of organisms that are evolutionarily interdependent, since algae are always present under natural conditions in the rhizospheric and root zones of higher plants, and there are usually more algae in the plant rhizosphere than in the soil around them, which is indicative of the symbiotic nature of their correlations [3, 4].

Our objective here was to study the reciprocal influence of chlorella and certain representatives of higher plants when cultivated in the same atmosphere of a closed system. In order to demonstrate better the reciprocal influence by means of discharge of gases, one must increase the concentration of such discharges, determine the conditions of combining chlorella and higher plants with respect to carbon dioxide content in the atmosphere and to prolong their joint cultivation. The first requirement is met by having a small volume of air per unit biomass. As we know, the optimum concentrations of carbon dioxide are not the same for chlorella and higher plants, and they differ by a factor of 10. For this reason, we first studied the correlation between concentration of carbon dioxide in the atmosphere and rate of its uptake by wheat plants in the ranges of 0.1-0.5, 0.5-1.0, 1.0-1.5 and 1.5-2.0%, with oxygen content of 20.6 to 22.0%. We tested carbon dioxide uptake in each of the above ranges for 24 h. As shown by the results of our experiments, with increase in concentration of carbon dioxide from 0.1 to 0.5% there is increase in rate of its uptake. Further increase in concentration of carbon dioxide up to 20.0% did not have an appreciable effect on rate of uptake by plants. It must be stressed that this function, like all of the subsequent ones, was obtained when plants were cultivated with continuous illumination.

The duration of continuous joint cultivation of plants and algae is determined by the range of concentrations of oxygen and rate of build-up thereof in the system's atmosphere, within which no inhibitory effect is observed of an excess or shortage thereof on the process of photosynthesis. The intensity of carbon dioxide uptake by chlorella is directly related to the concentration of oxygen in the gas phase: with increase in content thereof there is decrease in intensity of photosynthesis [5]. The top range of oxygen content in the atmosphere constitutes 23-25% for a number of vegetable plants [6], while the bottom range is 2.5-5.0% [7]. There are also data to the effect that the influence of concentration of oxygen on photosynthesis of higher plants depends on cultivation conditions. For example, it was shown that lowering the temperature and increasing the concentration of carbon dioxide attenuate the inhibitory effect of high concentrations of oxygen. For this reason, we first determined the rate of carbon dioxide uptake by the plants studied as a function of oxygen and carbon dioxide content in the atmosphere.

Within the tested range, oxygen content did not have an effect on uptake of carbon dioxide by both plant species (Table 1, Figure 1).

Table 1. Rate of CO_2 uptake by wheat plants with different concentrations of oxygen and carbon dioxide in the atmosphere

Level in atmosph., %		Uptake of
O_2	CO_2	CO_2, ℓ/day
10–12	0.5–1.0	3.03±0.09
10–12	1.5–2.0	3.35±0.19
20–22	0.5–1.0	2.77±0.00
20–22	1.5–2.0	3.11±0.14

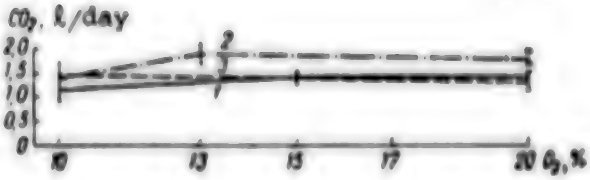

Figure 1.
Rate of CO_2 uptake by radish plants with different concentrations of oxygen in the atmosphere
1) 10-15-day-old plants
2) 15-20 day-old "
3) 20-25 " " "

Thus, the demonstrated dependence of intensity of photosynthesis on carbon dioxide content in the atmosphere enabled us to determine the range of it concentrations that would provide for normal vital functions of both the higher plants and chlorella when raised in the same atmosphere. The absence of effect of low oxygen concentration on photosynthesis of higher plants made it possible to prolong significantly the time of continuous joint cultivation of the components studied in the same atmosphere without partial or total replacement thereof.

Methods

The study of mutual influence of higher plants and chlorella was pursued on an installation, the diagram of which is illustrated in Figure 2.

This installation consists of a microalgal reactor with receiver and three pressure chambers for higher plants, one of which was combined with the reactor into one gas line, while the other two served as a control. The chambers and reactor are equipped with the necessary systems and devices for prolonged continuous cultivation of plants, measurement and regulation of the main parameters, both in autonomous and combined modes. In each chamber, the planting area constituted 0.1 m^2 and air volume was 60 ℓ. The volume of algal suspension constiututed 1 ℓ, with 0.15 m^2 illuminated reactor surface. Overall air volume of the system was 90 ℓ, illumination of plants and the suspension constituted 100 W/m^2 FAR [expansion not known].

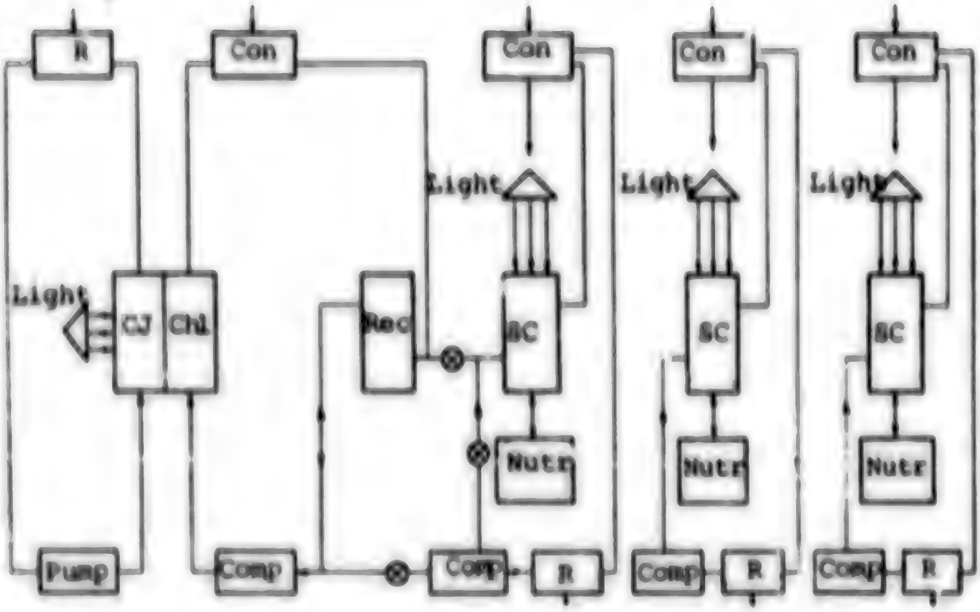

Figure 2. Diagram of installation. Explanation given in the text.

Key:

R) refrigerator	SC) sealed [pressure] chamber for higher plants
Con) condenser	Nutr) nutrient solution
CJ) cooling jacket	Chl) chlorella
Rec) receiver	Comp) compressor

In the tests, we used Strela spring wheat plants, pinkish-red radish and chlorella (Chlorella Sp-k). Up to the age of 19 days, the wheat plants were raised in an open device, then put in the pressure chamber, where they remained up to the age of 36 days. At this time (from the age of 20 to 36 days) biomass increment was relatively constant, constituting about 3 g dry substance per 100 plants per day. Radish seedlings were also kept in the open installation up to the age of 10 days, then put in the sealed chamber where they continued to grow to the age of 28 days. The concentration of carbon dioxide was held at 1 to 2% and oxygen at 10 to 22%. Before placing the components under study in the same gas line [system], we studied the intensity of carbon dioxide uptake and oxygen output by chlorella and the higher plants when raised under autonomous conditions. Wheat and chlorella were held in the same atmosphere for 3 days. Overall duration of joint cultivation of radishes and chlorella was 17 days. We lowered oxygen content every 3 days to 10% by pumping nitrogen through the system. We studied the effect of the common atmosphere not only on plant growth, but their development. In all of the experiments we conducted, along with examination of gas exchange in the system we determined chlorella productivity according to biomass increment.

Results and Discussion

Joint cultivation of chlorella and wheat in the same atmosphere did not affect their uptake of carbon dioxide, and photosynthesis of both components in the autonomous mode of cultivation did not change after cultivation in the same atmosphere (Table 2). The obtained data characterize photosynthesis and growth of wheat plants only for the tested period of time, during which the plants were at the same phase of development.

Table 2. Rate of carbon dioxide uptake by chlorella and wheat plants in the case of autonomous and joint cultivation in the same atmosphere

Cultivation	Chlorella		Wheat	
	cultiv. time, h	CO_2 uptake, ℓ/day	cultiv. time, h	CO_2 uptake, ℓ/day
Autonomous	4.0	2.88±0.12	14.5	3.16±0.17
Joint	42.0	2.96±0.54	42.0	3.18±0.62
Autonomous	7.5	3.24±0.13	7.5	2.61±0.17
Joint	11.5	3.12±0.11	11.5	3.07±0.11
Autonomous	13.0	3.04±0.58	13.0	2.53±0.37

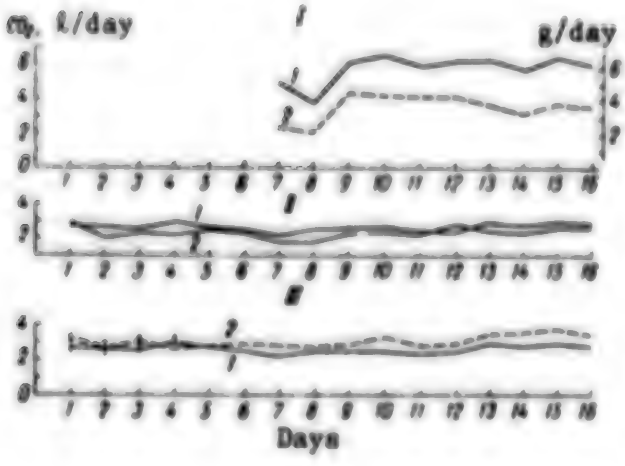

Figure 3.
CO_2 uptake by radish and chlorella with autonomous and joint cultivation in the same atmosphere
I) overall CO_2 uptake by radish and chlorella (1) and chlorella productivity in autonomous mode (2; g/day)
II) CO_2 uptake by radish plants with with autonomous cultivation in chamber No 3 (1) and No 2 (2)
III) CO_2 uptake by radish plants when cultivated autonomously (1) and jointly with chlorella in the same atmosphere (2)

Figure 3 illustrates the mean daily uptake of carbon dioxide by chlorella and radish plants when cultivated together, as well as productivity of chlorella according to dry substance increment. Overall uptake of carbon dioxide coincided entirely with the trend of the curve of productivity of chlorella according to dry substance. Analysis of the data illustrated in

Figure 3 shows that uptake of carbon dioxide by radish plants raised in the same atmosphere as chlorella was virtually the same as when raised autonomously. Phenological observations of growth and development of radish plants cultivated in the same atmosphere as chlorella and under autonomous conditions failed to demonstrate any substantial changes in development. We only observed earlier bolting (by 1-2 days) of experimental plants.

After the experiment, we measured plant weight and determined the structure of the level. Wet and dry biomass of radish plants raised under autonomous conditions and in the same atmosphere with chlorella was virtually the same (the differences were unreliable).

In view of the fact that the plants had started to bolt intensively at the time they were harvested, growth of the root crop was retarded in both the experiment and control, and this is probably related to the fact that there was continuous illumination.

The results of these experiments allow us to conclude that under our test conditions gas discharge by chlorella did not have an appreciable effect on uptake of carbon dioxide by wheat and radish plants or on their biomass increment. In turn, the gas discharge of higher plants did not affect vital functions of chlorella. Consequently, we can voice the preliminary conclusion that chlorella and the representatives of higher plants studied do not have an appreciable reciprocal inhibitory effect when cultivated in the same atmosphere, and for this reason they may be considered as biologically compatible components of the photoautotrophic element of future bioregenerative human life support systems.

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METHODS

UDC: 616.28-07:617.761-009.24

GENERALIZED NYSTAGMOMETRIC CHARACTERISTICS FOR DIAGNOSTIC PURPOSES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1980 pp 78-82

[Article by M. M. Levashov and A. I. Tumakov, submitted 4 Apr 78]

[Text] Nystagmometric diagnostics amount to comparing "output" reactions induced by the same perturbances at the "input" of the system studied. It is assumed that there is a certain "norm" (or background), a difference from which is evaluated as a sign of pathology (or influence of a factor studied).

In most cases, the comparison is made by assessing the probability of error made when relating the compared reactions to various sets. It is not always by far that the changes in nystagmus, when assessed according to a single parameter, are statistically significant and reliably beyond the range of normal variations. Yet we know that deviations may consist not only of a significant change in some nystagmometric characteristics, but change in correlation between parameters. In other words, there may be impairment of correlations, according to which one can demonstrate a reliable deviation of reactions from normal, although each of the parameters individually would not differ from the norm.

Generalized evaluation of the nystagmic reaction (or reactions), which takes into consideration the statistical relationship between parameters of nystagmus [1-3], could be used as the basis for solving the problem of demonstrating such differences. It was proposed that the so-called distance (quadratic form of deviation of random [sampled] values of parameters from the corresponding means) be used as a gage of deviation from the norm. One can judge not only the reliability of a difference (i.e., probability of erroneous judgment), but trends in direction of changes in repeated tests, if necessary, according to this distance. Two approaches have been developed, which differ in their concrete objectives. In the first case (first type of diagnostics), a "normal" set of nystagmograms is described, in which each individual reaction is presented as a generalized evaluation of two or more parameters (for example, three-dimensional distribution,

which is constant for duration of nystagmus, mean rate of slow component and mean frequency). An individual nystagmic reaction, which must be given a diagnostic evaluation is compared to this distribution, i.e., determination is made of the reliability of its difference at a specificed confidence level [1, 4]. In the other case (second type of diagnostics), it is not an individual nystagmic reaction that is the object of diagnosis, but a pair of reactions recorded on a subject, for example in the same caloric test on the right and left. In this case, the generalized evaluation takes into consideration the statistical relations existing between analogous parameters in reactions going in different directions. Accordingly, the norm (or background) is a sample, in which each date is represented by a pair of reactions, while the distance, which serves as a gage of difference, indicates the extent to which a given subject differs from the "norm" with regard to the sign of correlations between analogous parameters of reactions elicited by the same stimulation of different labyrinths. As related to cold caloric nystagmus, this procedure of nystagmometric diagnostics (statistics of the norm, conversion of initial samples, formula for calculation of distance, deciding diagnostic rule) was described comprehensively before [1].

Our objective here was to demonstrate the possibility and prospects of using the second type of diagnostics for the purpose of evaluating optokinetic reactions. Optokinetic nystagmus (OKN), which has long been an object of investigation in special diagnostic studies [5], is acquiring increasing significance in vestibulometric studies as its close links with the vestibular system are being demonstrated [6-8]. Evidently, recording and quantitative evaluation of OKN will become mandatory elements of the vestibulometric diagnostic complex used in occupational screening in the very near future. For this reason, it is a pressing task to determine the deviations of OKN from normal, including asymmetries, i.e., to demonstrate pathological asymmetry beyond the range of physiological asymmetry, which is not uncommon. Moreover, we should like to call the reader's attention to a convenient graphic procedure, with which calculations involved in the second type of diagnostics can be simplified.

Methods

We studied 39 children ranging in age from 3 to 7 years who were not suffering from vestibular dysfunction. The methods and detailed description of examining them were described previously [3]. The optokinetic stimulus (white spots of the same size randomly scattered on a black background), which moved in the horizontal plane, was projected on a screen that occupied a significant part of the field of vision (120° horizontally and 70° vertically). The subjects were merely asked to look at the screen, and no other instructions were given. We submit below the results of processing 234 electronystagmograms (ENG) of OKN recorded at three stimulus rates, 4, 10 and 20°/s. Primary processing of the ENG consisted of

finding 2 characteristics for each reaction on a 20-s segment: the mean rate of the slow component (RSC) and number of jerks [beats]. The number of jerks measured in such segments corresponds to a 20-fold increased mean frequency, and for this reason we call this parameter the frequency in the tables and charts. Further processing was performed on an M-4030 computer. Each sample consisted of 39 pairs of analogous characteristics (for example, RSC) obtained in left and right OKN at the same stimulus rate. Thus, we obtained 6 samples (RSC and frequency with three stimuli) and for each of them we plotted joint distribution [1], determined the coefficients for the formula of quadratic deviation (i.e., distance) and 95% confidence interval for the norm (illustrated graphically).

We consider it necessary to mention that one should examine the norm (or background in each specific instance as related to the methods and other distinctions of the study, and it is expressly from this point of view that one should approach the norm described below. Further, the OKN norm for a child is unquestionably different from that of an adult. In this respect, our report may be of interest, not only as an example of an untraditional nystagmometric approach, but in connection with some of the distinctions of the OKN of children. It is known that the quantitative characteristics of OKN are substantially related to the extent to which the subject actively participates in visual tracking. An adult can be instructed to attentively examine a moving stimulus or, on the contrary, his attention can be distracted from tracking. We then obtain two qualitatively and quantitatively different OKN: the parameters of the second OKN depend much less on higher levels of the central nervous system, which correct eye movements and make the RSC conform with the speed of the stimulus. In addition, this nystagmus is more susceptible to influences of the vestibular system. It appears that in children, under the conditions of the methods we used, the reactions were closer to the second type of OKN.

Results and Discussion

The Table lists the results of traditional statistical processing (mathematical expectation and standard deviation (for the parameters of right (X) and left (Y) optokinetic reactions, as well as a sample made up of differences in parameters obtained for each pair of reactions. We also listed the coefficients of correlation ($r_{X,Y}$) between sets [samples] X and Y. To avoid ambiguity, let us indicate that the result of individual measurement of one OKN (for example, mean RSC of a right OKN) is designated as X, therefor X is the mean of the means. The same applies to reactions directed to the left. In the Table, we also list the coefficients of regression $R_{Y/X}$ and free terms of regression equations $B_{Y/X}$. The three coefficients (a, b and c) in the last columns of the table are referable to "second type of diagnostics," which we shall discuss below.

It is noteworthy that there is a distinct difference in behavior of two parameters of nystagmus, RSC and frequency. A significant positive

correlation between left and right OKN was demonstrated with all three stimuli with regard to frequency, whereas a marked correlation for RSC was demonstrated only with a stimulus of 10°/s; it was insignificant with 20°/s and lacking with 4°/s. In other words, the rate of the optokinetic stimulus had a different effect on the tonic and rhythmic systems of nystagmus.

The quadratic deviation of distance for two-dimensional distribution was calculated with the following formula:

$$d = a\Delta_1^2 + b\Delta_1\Delta_2 + c\Delta_2^2$$

where Δ_1 is the difference between the value of the parameter studied in right OKN and corresponding mathematical expectation, Δ_2 is the same for left OKN in the subject examined, while a, b and c are the coefficients listed in the table for each of six samples made up of pairs of characteristics. These coefficients were obtained as a result of converting the initial paired OKN samples to apply to the second type of diagnostics [6].

Main statistics of OKN samples at three rates of optokinetic stimulus

Stimulus, degrees/s	$\bar{X}$	$\bar{Y}$	$(\bar{X}-\bar{Y})$	$r_{X,Y}$	$R_{Y/X}$ $B_{Y/X}$	a	b	c
			RSC					
4	4,28 (0,82)	4,33 (0,90)	−0,055 (1,318)	−0,178*	−0,196 5,147	1,546	0,502	1,280
10	10,85 (2,18)	11,04 (2,00)	−0,192 (1,477)	0,753	0,692 3,540	0,487	−0,799	0,587
20	20,52 (1,68)	20,59 (2,19)	−0,067 (2,257)	0,341	0,447 11,426	0,102	−0,210	0,236
			Frequency, number of jerks					
4	5,26 (2,12)	5,72 (3,13)	−0,462 (1,570)	0,890	1,311 −1,175	1,070	−1,293	0,493
10	14,59 (6,25)	14,51 (5,83)	0,077 (3,557)	0,829	0,773 3,235	0,082	−0,145	0,094
20	22,79 (8,37)	22,41 (8,93)	0,385 (5,923)	0,768	0,819 3,734	0,035	−0,050	0,030

Note: Standard deviations of samples are given in parentheses; the asterisk indicates an unreliable difference from zero.

We must make several simple calculations to determine whether a pair of the subject's reactions differs from the "norm" with regard to the sign of correlations between analogous parameters of these reactions. We have to find the mean RSC and number of jerks per 20-s segments of the reactions in each of two ENG of the subject's OKN recorded with the same stimulus rate. We then have to calculate Δ_1 and Δ_2 as the difference

between the obtained values and corresponding mathematical expectations. For example, Δ_1 equals (if the evaluation pertains to RSC) the difference between mean RSC of the subject's right OKN (X_1) and arithmetic mean of RSC of the right OKN with a given stimulus (i.e., $\bar{X}$, see Table). The values found for Δ_1 and Δ_2 with the corresponding coefficients, which are listed in the Table, must be substituted in the formula, and then d is calculated (distance). With $d \geq 6.0$, the probability of error in referring the pair of OKN to those differing from normal would constitute less than 5%.

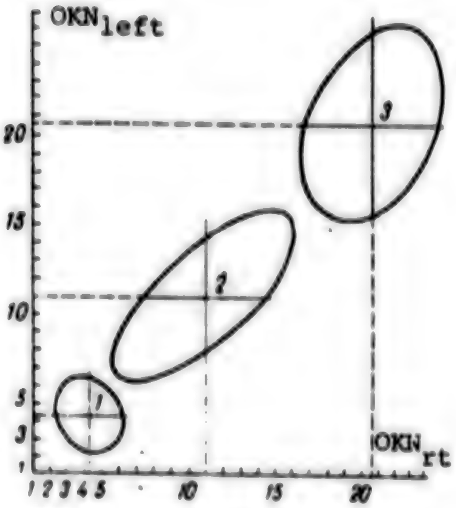

Figure 1.
Rate of slow component of OKN (mean RSC for 20-s segment of OKN) with different rates of optokinetic stimulus. Generalized characteristics are given for three samples each consisting of 39 pairs of analogous parameters in differently directed reactions (x-axis, SRC for right OKN; y-axis SRC for left OKN). Here and in Figure 2, the ENG's were plotted for three stimulus rates: 4 (1), 10 (2) and 20°/s (3). The straight lines refer to coordinates of mathematical expectation, the oval circumscribed zones refer to 95% confidence level in each sample.

If there is no need to know the exact value of d (for example, when it is sufficient merely to determine that it differs from "normal"), one can use the graphs illustrated in Figures 1 and 2. After finding the point of intersection of coordinates for the parameters of a pair of reactions in a given subject, one can make a diagnostic decision according to the location of this point, in or out of the zone circumscribing a 95% confidence level. Whenever the point is outside this zone, the decision is made that the tested pair of OKN differs reliably ($P<0.05$) from the "norm." This procedure may be particularly useful in mass screenings, since it makes it possible to do without making calculations using the formula.

This procedure may also be useful in selecting an optimum examination and informative parameters of the reaction. Thus, the stimuli we used apparently differ in significance to the system under study. This is indicated, for example by the dependence of the individual physiological RSC asymmetry on the rate of the stimulus. Let us explain this with an example. Since the position of any point of intersection of the coordinates, which does not exceed the boundaries of the circumscribed zone must be interpreted as a sign that it belongs to a normal set, let us find in each zone a point, for which X and Y will differ enough, i.e., let us find reactions that are in the normal range and,

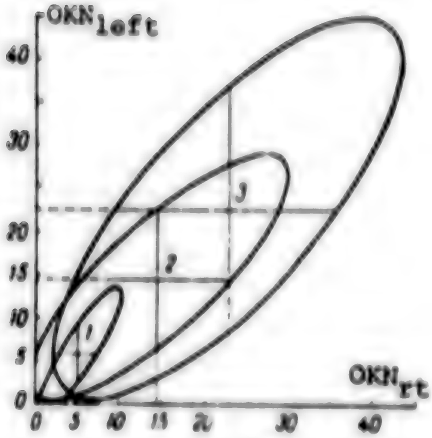

Figure 2.
Frequency of OKN (jerks per 20-s OKN) at different rates of optokinetic stimulus. Generalized characteristics are given for three samples (x- and y-axes, right and left OKN, respectively)

at the same time, asymmetrical for RSC. With a stimulus of 4°/s, we can select a point with coordinates X = 2.5 and Y = 5.0. The absolute difference in RSC in such a pair of OKN will be 2.5°/s, and the relative difference, expressed as percentage of sum of RSC, will reach -33%. Analogously, let us evaluate a pair of reactions with a stimulus of 10°/s: at the point with coordinates X= 5.5 and Y = 7.5, the absolute difference will be -2.0°/s and relative difference -15%. With a stimulus of 20°/s, at the point with coordinates X = 16.5 and Y = 19, where the absolute difference is -2.5°/s, the relative difference is -7.3%. In other words, as we move from low rate of stimulus (4°/s) to the highest (20°/s) there is an appreciable decrease in "normally" permitted relative asymmetry of OKN referable to RSC; for each distribution there is its own maximum level asymmetry. It is another matter for frequency (see Figure 2). Here, the point with coordinates of, for example, X = 3.0 and Y = 5.5 belongs to an equal extent to all three distribution; in such a pair, the relative frequency asymmetry will be -29%, i.e., quite significant asymmetry is "normal" for OKN evoked by any of the three stimuli.

Hence, it is better to use evaluation according to RSC, rather than frequency, whenever the object of the study is asymmetry of reactions, and of the stimuli used, the most advantageous will be the one with a rate of 20°/s, since physiological asymmetry is minimal with this rate. The distribution of RSC is less variable than distribution of frequency; for this reason, the frequency is not a very suitable parameter for assessing OKN asymmetry. Its variability is so significant that all three zones of 95% confidence level are superimposed over one another. These data compel us to adopt a cautious attitude toward diagnostic tests based only on evaluation of frequency. This suggests the practical conclusion that a comprehensive evaluation must be made of nystagmic reactions when there are problems related to diagnostics, i.e., mandatory consideration of properties of these reactions due to both rhythmic and tonic systems [9].

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UDC: 628.315:613.693

UPGRADING EFFICACY OF MEMBRANE TECHNIQUES FOR REGENERATING WATER FROM URINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 82-83

[Article by B. A. Adamovich, V. D. Volgin, N. M. Nazarov, Yu. Ye. Sinyak and S. V. Chizhov, submitted 3 May 78]

[Text] The most effective of all membrane [diaphragm] methods of regenerating water from urine are those involving evaporation through membranes and back osmosis. Since urine is an aqueous solution, most constituents of which are not volatile or minimally so, evaporation through a membrane, which is not semipermeable, yields water of a good quality that only requires some additional treatment. In this case, polymer film or porous diaphragms made of, for example, cermet [metal ceramic].

Since semipermeable membranes based on acetate cellulose retain up to 99% sodium chloride, while polyamide membrane retain up to 80-90% urea, there was a real possibility of developing a competitive system of regenerating water from urine on the basis of reverse [back] osmosis.

Any membrane consists of a porous diaphragm [wall, barrier], on the surface of which the process of separation of water from other urine components takes place. The concentration of these components increases (concentration polarization), and if they are slowly diverted from the interface a sediment is formed. This sediment accumulates on the membrane surface and is deposited in its pores, which leads to rapid decrease, not only in rate of the process but in selectivity of separation of the solution. For example, in a device where urine is evaporated through porous cermet plates 0.15 mm in thickness with mean pore size of 2 μm, output decreased by more than 4 times in 20 days of continuous operation. However, formation of a sediment did not affect the quality of the obtained water: biochromate oxidizability constituted 100 mg O_2/ℓ, permanganate oxidizability 9.75 mg O_2/ℓ, ammonia content was 8.52 mg/ℓ, odor was rated at 5 points and transparency 30 cm. In the case of back osmosis, there was the same decline in output, which was associated with gradual increase in stained layer of sediment containing urea and sodium chloride on the filter.

Thus, one of the main prerequisites for improving the efficiency of membrane devices amounted to taking steps precluding formation of a sediment. This can be achieved only if a solution containing components in amounts far from saturation is delivered to the apparatus. Since urine is a virtually saturated solution with respect to many constituents and left to stand there often spontaneous precipitation of sediment, one of the mandatory steps is to lower the concentration of urine components. The possibility was considered of partial isolation of the sediment from urine by cooling it and altering the pH. According to the results of 6 tests, cooling urine to 5°C led to precipitation of 4.83 ± 0.95 g/ℓ sediment, while a change in pH to 10.0 led to formation of 10.6 ± 0.8 g/ℓ sediment.

Thus, cooling and alkalinization made it possible to decrease by almost 40% the overall concentration of urine constituents.

Since two-stage processing is technically more complicated and does not rule out the possibility of decomposition of urea, it was expedient to limit ourselves thereafter to one stage, cooling.

In both cases, the permissible coefficient of extraction was in the range of 65-90%. Moreover, the urine concentrate obtained after extracting 50% water from it and submitting it to the same cooling, enabled us to extract another 85-90% of water without precipitations.

In view of the fluctuations in composition of urine, these figures may be lower in some cases. For this reason, it is recommended to use an extraction coefficient of no more than 50%. In this case, it is expedient to run the regeneration process in 2 stages: primary extraction of up to 50% of the water and secondary extraction of water up to 50% from the urine concentrate, as a result of which total extraction will constitute 75%. The effectiveness of such treatment was tested on a laboratory unit with an evaporator made of porous cermet.

Urine was stored in the refrigerator for 24 h, after which the formed sediment was filtered out on a viscose-chlorine filter. The filtered urine was decanted into the unit and we ran the separation process holding the water extraction coefficient at close to 50%.

For the first 4 days, the productivity of the unit dropped to about one-half, which could be related to stabilization of membrane properties. At the second stage, which lasted 16 days, output remained constant. The overall coefficient of water extraction constituted 74%.

Thus, as a result of this experiment, it was established that one can keep productivity of the unit stable for a long period of time. Analogous results were obtained when water was regenerated by the method of back osmosis. Here, the limiting factor was obstruction of membranes by the sediment, which formed as a result of corrosion of equipment elements and microbial contamination of unpreserved urine.

The difficulty involved in selecting a preservative for urine, as related to physicochemical regeneration systems, lies in the fact that the preservative must stabilize urine composition and bind into a complex volatile and usually highly toxic substances, in addition to a decontaminating action. The preservative must be nontoxic, and its phase (solid, liquid, gas) must be determined by the method used to process urine. In addition, the preservative must not lose its antibacterial properties upon contact with the materials of the system and cause corrosion of the latter. It is also undesirable for a sediment to form from the preservative proper.

Urine can be decontaminated by physical, biological and chemical methods, or combinations thereof. Physical methods include heat and ultrasound, ultraviolet radiation, ionizing radiation and exposure to magnetic fields. However, these physical methods all have a common flaw: they do not have an aftereffect on microflora. Thus far no biological method has been developed for preservation that would be based on antagonism of microorganisms. The chemical method of preserving liquid waste best meets the above requirements. Putman [1] recommends the use of a mixture of sulfuric acid, chromium trioxide and copper sulfate as a urine preservative. Sulfuric acid changes ammonia salts of urine into stable compounds, precluding access of ammonia into regenerated water. At the same time, as a preservative the acid could cause formation of new compounds as a result of dissociation of complex and, first of all, nitrogen-containing, components of urine, which worsen the chemical parameters of regenerated water. We shall list here some of the parameters of quality of water regenerated from urine by the distillation method as a function of its reactivity. The most important parameters of quality of regenerated water are the amount of ammonia nitrogen and bichromate oxidizability. Bichromate oxidizability of regenerated water decreases from 6.0 to 5.0 with decrease in pH of initial urine, and it is lowest at urine pH in the range of 5.0 to 3.0. At urine pH of less than 3.0 the oxidizability of recovered water increases sharply. The findings are different with regard to ammonia content of regenerated water: decrease in amount thereof with decrease in pH of initial urine and increase with increase in pH. Urine pH in the range of 3.0 to 5.0 is the optimum for recovering the best quality of water; however, at urine pH of 4.0-5.0 conditions develop that favor development of lower fungi. When the pH is lowered to 3.0, a decontaminating effect lasting up to 3 months is obtained. In the absence or inadequate efficacy of preservative, the water regenerated from urine will have bichromate oxidizability of several hundred milligrams oxygen per liter, and ammonia nitrogen up to several thousand milligrams per liter. Such water requires substantial additional treatment.

Thus, membrane separation methods can be used with success to regenerate water from urine after reliable methods are developed for preserving urine and removing mechanical and colloid impurities from it.

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UDC: 612.216-087

USE OF POLYURETHANE FOAM DEFORMATION SENSOR TO RECORD RESPIRATORY ACTIVITY

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 84-85

[Article by V. I. Bredov and V. S. Baranov, submitted 20 Feb 79]

[Text] Various types of sensors are used to record respiratory activity. Special requirements are made of such devices in the case of biotelemetry studies: they must be small in size and weight, reliable, simple in construction, convenient to use, etc.

The sensor developed by V. S. Baranov [1] has some substantial advantages over other known types [2, 3]. It is highly sensitive over a wide range of strain loads. The level of the output signal is linearly related to the force ex-rted on it, and it is sufficient for direct recording without using amplifiers of electric signals. The sensor is based on elastic, spongy material, polyurethane foam (porolon) with current-conducting material on the pore surface, current-conducting carbon black or electrode paste. In the latter case, the sensitivity of the sensor is somewhat greater. The elastic properties of the sensor are built in the actual base of the strain-sensitive element, which simplifies the construction substantially and increases the reliability of the unit.

Figure 1 illustrates the ohmic resistance of the strain-sensitive element as a function of magnitude of applied load.

In order to test the possibility of using this sensor to examine respiratory function, we recorded human pneumograms with the subject in a calm state. Figure 2 illustrates the tracing of the respiratory curve. We also recorded respiratory activity of experimental animals (dogs). Figure 3 illustrates samples of such tracings.

The simplicity of design of the sensor makes it possible to use it in various physiological experiments, when the parameter measures is related to mechanical loads or can be transformed into them, for example when recording motor activity in actography, taking respiration tracings during submersion under water or ascent to high altitudes.

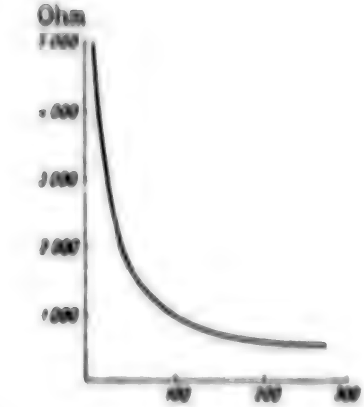

Figure 1.
Change in ohmic resistance of a sample of strain-sensitive element as a function of applied force. X-axis, load (g); y-axis, resistance (in ohms)

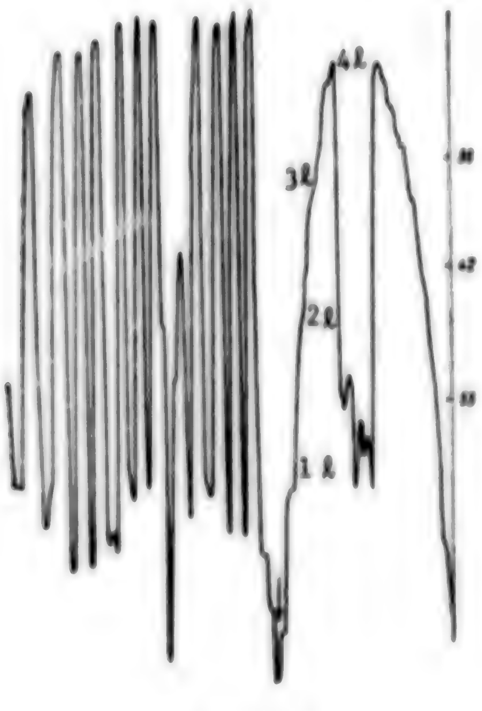

Figure 2.
Human pneumogram with individual in a calm state, standing. The arrow shows deep expiration and the numbers refer to measured inspiration

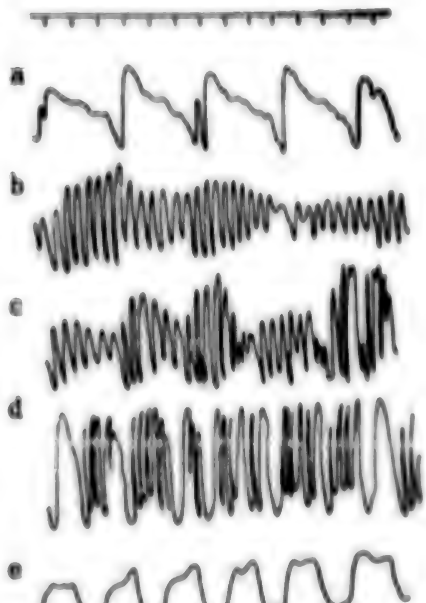

Figure 3.
Pneumogram of experimental animal in the presence of different functional states

a) standing, calm state
b) with delivery of conditioned sonic stimulus
c) during movement (depressing pedal with paw) during exposure to conditioned sonic stimulus
d) pain stress (electrodermal stimulation)
e) experimental neurosis.

X-axis, time (1-s graduation)

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BRIEF REPORTS

UDC: 612.273.2+612.014.477-063].017.2

INFLUENCE OF SPECIFIC CONDITIONING ON WHITE RAT RESISTANCE TO THE COMBINED EFFECT OF HYPOXIA AND -G ACCELERATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 85-86

[Article by M. A. Kolesov, submitted 28 Jun 77]

[Text] Our objective here was to make a comparative study of the efficacy of specific conditioning methods for the purpose of enhancing resistance to the combined effect of hypoxic hypoxia and negative accelerations.

Methods

The studies were conducted on 183 male mongrel white rats weighing 180-240 g. The animals were divided into five groups. The first consisted of rats rotated once on a centrifuge (65 cm arm), placed in a PBK-53 pressure chamber 5.6 m^3 in size, at an "altitude" of 6500-7250 m, without prior conditioning. The rotation generated accelerations of 2.4 units in the pelvis-head direction lasting 48 min. The second group of rats was submitted to accelerations under the same conditions in a head-pelvis direction; the third group of animals underwent daily conditioning for hypoxia for 1-3 months in the pressure chamber prior to rotation at accelerations of 2.4 units in the pelvis-head direction at high "altitude." Conditioning began with initial "ascent" to 4000 m, then the "altitude" was gradually increased and reached 8000-9000 m at the end of the training period. The rate of ascent and descent constituted 30 m/s. The time the animals spent in the chamber increased from 1 to 4 h. The fourth group of rats was exposed repeatedly (at intervals of 1-2 days) to the combined effect of accelerations and hypoxia over a period of 35-40 days. Here, the "altitude" was gradually increased from 3500 m at the start of the experiment to 6000-7000 m at the end, while rotation time increased from 5 to 45-50 min. In the fifth group, the rats were rotated on the centrifuge for 1 h daily for 3 weeks under ordinary atmospheric conditions. The fourth and fifth groups were rotated in accelerations of 2.4 units in the pelvis-head direction. During rotation, the rats were kept in separate box-cages.

Upon conclusion of conditioning, the animals of the third, fourth and fifth groups, like those of the first group, were rotated once at a high "altitude." Animal survival served as a criterion of endurance. In the rats that survived after the experiments and in 20 intact animals we determined organic blood filling. Immediately after the tests, the rats were sacrificed by rapid immersion in liquid nitrogen. We took 100-mg samples of organs (brain, heart, lung, liver, kidney, spleen, femoral rectus muscle) and homogenized them in 8 mℓ 0.007 M aqueous ammonia solution, in which all of the blood hemoglobin changed to oxyhemoglobin. We diluted 0.04 mℓ whole blood in the same amount of the same solution. The homogenates were centrifuged in a TsVR-1 centrifuge at 18,000 r/min for 20 min, after which the clear solution was decanted into a cuvette 1 cm in diameter, then determined extinction at wavelengths of 580, 605 and 630 nm using an SF-14 spectrophotometer [11]. We assayed blood (in mℓ/100 mg tissue) using the following formula:

$$\frac{[E_{580} - E_{605}] - [E_{605} - E_{630}]}{E_{580} - E_{605}} \cdot 0.04,$$

where the dividend is extinction of tissue and divider is extinction of blood. The results were submitted to statistical processing with the use of Student's criterion.

Results and Discussion

The results of the experiments revealed that only 10 (22.8%) out of the 44 rats in the first group survived after single rotation at an "altitude" of 6500-7250 m for 38 min; all 15 rats of the second group, rotated in the head-pelvis direction, survived; 14 (46.6%) out of 30 animals conditioned for hypoxia survived; 21 (61.7%) out of the 34 rats in the fourth group survived and 27 (77.1%) out of 35 survived in the fifth group.

There was increased filling of the brain with blood in all groups. The maximum increase was demonstrated in unconditioned animals rotated in the pelvis-head direction (by 39%). In the conditioned rats of the fourth and fifth groups, there was appreciably less delivery of blood to the brain (by 22%) than in unconditioned ones.

The changes in filling of kidneys were similar. They were not in contradiction to the findings of other authors [1, 2], who observed a decrease in renal blood flow with separate exposure to acute hypoxia and accelerations. Statistically reliable increase in blood flow in the spleen was observed only in rats submitted to pelvis-head accelerations. It may be assumed that plethora of the spleen was in the nature of a reflex and related to some stasis of blood in the pulmonary circulatory system.

It can be concluded on the basis of these data that not only hypoxic, but circulatory hypoxia, which worsened even more delivery of oxygen to the

brain [3] as a result of impairment of cerebral hemodynamics and limited endurance of accelerations, were the cause of animal deaths after rotation in the pelvis-head direction.

The obtained data show that it is possible, in principle, to search for effective methods of specific conditioning to enhance resistance to the combined effect of acute hypoxia and gravitational accelerations.

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DISCUSSIONS

UDC: 612.821-057:656.7-051

DISTINCTIVE FEATURES OF CHANGES IN PSYCHOPHYSIOLOGICAL PARAMETERS OF CREWS OF CIVIL AVIATION HELICOPTERS AS RELATED TO WORK LOAD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 2, 1980 pp 86-89

[Article by Yu. N. Kamenskiy, submitted 1 Aug 78]

[Text] The wide use of helicopters in the national economy makes it increasingly important to use a scientifically substantiated and differentiated approach to setting standards with regard to work load for their crews. This involves, first of all, a study of the question of fatigability and efficiency of pilots as related to the intensity of the work [flight] load and effect on crew members of adverse flight factors [1-3]. Studies pursued by a number of authors [4, 5] have made it possible to substantiate flight load standards separately for helicopters with one and two pilots aboard. However, this did not take into consideration a number of other factors. Experience in operating helicopters has shown that one must take into consideration, in setting flight load standards, the influence on pilots of such factors as the industrial environment (noise, fibration, uncomfortable temperatures), location of base (main base, operational center, expedition) time of year and climate.

Heretofore, these questions were not covered in any detail in studies dealing with physiology of flying work in the Civil Aviation.

Methods

We observed the crews of Mi-4 (first series) and Mi-6 (second series) helicopters. The first series of observations was conducted in May at ambient temperatures of 18-25°C and the second in the northern regions of European USSR in April, at atmospheric temperatures of 2 to -15°C.

The crew members were examined 30-40 min before and 30-40 min after terminating flights. In all, we examined 20 members of Mi-4 helicopter crews and 66 of Mi-6 helicopter crews. The crew members of the Mi-4 helicopters made flights daily over the entire work week. The examinations before and after flights were also made daily. The crews of Mi-6 helicopters

worked at 1-2-day intervals during the week, with 3 to 7 h flying time daily. The crew members of the Mi-6 helicopters were divided into three groups according to daily flying time: the first group consisted of personnel with daily flying time of up to 5 h (24 people), the second with up to 6 h flying time (22 people) and the third, up to 7 h (20 people).

We studied the following parameters: critical fusion frequency (CFF), static tremorometry (ST), reaction to a moving object (RMO) and reproduction of a specified muscular exertion (RME). We studied the subjective evaluation by pilots of working conditions by means of anonymous questionnaires. The results were processed statistically using the criteria of Student.

Results and Discussion

In the pilots of Mi-4 helicopters, the base values of psychophysiological parameters changed inconsistently from day to day. Conversely, the postflight changes presented distinct weekly dynamics (Figure 1). After the first work day, there was a reliable increase in ST (by 79±9%) and percentage of RME deviations (by 88±20), as well as accuracy of RMO (by 54±12%). After the second and third work day, the postflight changes were considerably less marked. After completing the flights on the 4th day, we observed a reliable increase in ST and RME (by 78±10 and 150±14% of the base levels, respectively). On the 5th and 6th days, there was a reliable decrease in CFF (by 12±2 and 13±4%, of base values, respectively) and accuracy of RMO (by 56±9 and 52±7%). Thus, the dynamics of postflight changes in psychophysiological parameters were characterized by marked changes after the 1st flight day, decreased changes and relative stabilization after the 2d and 3d days, and a gradual second increase starting on the 4th day. The severity of changes in the parameters studied on the 1st and 6th days corresponded to grade III fatigue according to Ye. F. Polezhayev and V. A. Yepikhin [6].

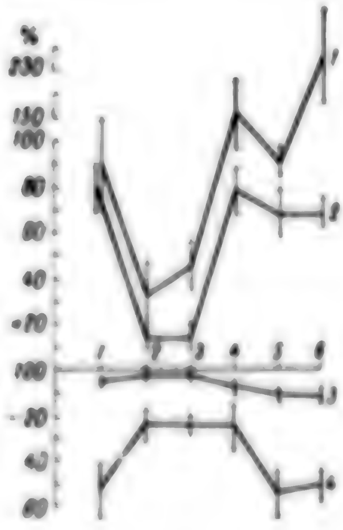

Figure 1.
Dynamics of changes in psychophysiological parameters of Mi-4 pilots in the course of a work week. X-axis, work days; y-axis, changes in parameters as related to initial levels.

Consequently, there was phasic change in functional state of the Mi-4 pilots during the work week: The first phase corresponded to the 1st day of work and was characterized by development of marked fatigue, which

could be the result of partial deconditioning for the work loads and working conditions during the preceding time off. The second phase, which coincided with the 2d and 3d work days, could be indicative of adaptation of the pilots to the work loads. If we use adaptation to refer to an increase in physiological capabilities and increase in performance [efficiency] [7], apparently there was the highest level of safety of flights during this period because of the human [personal] factor. The third phase began on the 4th day of flights, and it can be qualified as a manifestation of depletion of functional reserves, which could lead to diminished performance.

For expressly this reason, one should not recommend daily flights on helicopters for 6 consecutive days with daily flying time of 7 h. It is necessary to use a somewhat altered flight schedule. One of the variants could be to have flights for 3-4 days followed by 1-2 days of rest. Another variant could be based on the same schedule, but decreasing flying time on the 1st day after time off by 1-2 h.

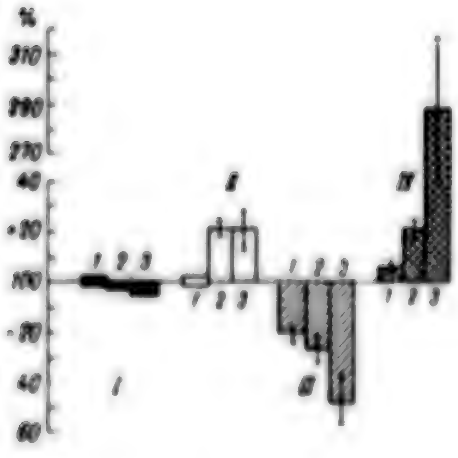

Figure 2.
Changes in psychophysiological parameters of Mi-6 pilots as related to different daily flying times

I) CFF — 1) 5 h flying time
II) ST — 2) 6 h
III) RMO — 3) 7 h
IV) RME

Analysis of the results of the second series of studies revealed that the changes in psychological parameters were insignificant in Mi-6 pilots flying up to 5 h per day. With up to 6 h flying time, reliable changes in parameters were demonstrated, as compared to both base levels and postflight findings in the first group: 27±4% decrease in accuracy of RMO, 20±3% increase in RME error, while ST increased by 21±3% (Figure 2). The most substantial changes were noted in crew members who flew up to 7 h per day: RMO accuracy decreased by 50±9%, RME error increased by 290±28% and ST index increased by 21±8% (see Figure 2). With flying time of up to 5 h daily, the functional state of crew members corresponded to grades I-II fatigue according to the classification of Ye. F. Polezhayev and V. A. Yepikhin; it was rated as grade II with up to 6 h flying time and characterized by early signs of fatigue, and as grade III with flying time of up to 7 h, which was characterized by marked fatigue.

Of course, development of fatigue was associated with diminished performance. Under ordinary flying conditions, this does not necessarily have a substantial effect on quality of decision making and piloting, but when flying conditions are more complex (poor visibility, snow, "bumpy" air, technical malfunction) there could be preconditions for flight incidents. Instances of loss of spatial and geographic orientation by pilots, appearance of spatial illusions in difficult situations have been described [8-10].

It is known that pilots develop fatigue not only under the influence of flight work, but exposure to concomitant factors, particularly vibration and noise [1, 5, 11-13]. The vibration and noise levels may reach high intensities in the crew's cabins of modern helicopters [14-16]. This warrants the assumption that vibration and noise did not play the last role in development of fatigue among the crew members of Mi-4 and Mi-6 helicopters. Special mention should be made of the possible influence of vibration, as confirmed by the drastic changes in accuracy of RME with flying time of 6 h or more. The RME is probably the most adequate of the set of parameters used with respect to vibration, since the afferent element of the arc of this reflex begins at the mechanoreceptors of the motor analyzer. At the same time, the findings of a number of studies suggest that vibration is a specific stimulus for mechanoreceptors [17-19].

The assumption that vibration plays a significant role in development of fatigue is also confirmed by the results of analysis of subjective data. All of the pilots rated vibration and noise as the most unpleasant factors. Vibration was rated even worse than noise (30.7% of the answers); noise was more unpleasant than vibration for only 10.5% of those questioned; noise and vibration were equally unpleasant for 58.8%.

Fatigue is the natural result of any work. The question is only of the degree of fatigue. If we were to assess the postflight changes from this position among the crew of Mi-6 helicopters involving different daily flying times, a 6-h/day standard can be considered warranted. The question of a 7-h daily flying time can be answered in the affirmative provided there is further improvement of work schedule for helicopter crews and decrease in their exposure to deleterious flight factors, first of all vibration and noise.

Thus, there must be differentiated determination of work standards aboard helicopters of the Civil Aviation and it must take into consideration working conditions (noise, vibration, other adverse flight factors). Differentiated and scientifically substantiated standards for flying time aboard helicopters will reduce pilot fatigue and provide for a high performance, which will be instrumental in further increase in safety of flights.

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CURRENT EVENTS AND INFORMATION

UDC: 57+61](15):002.66

DATA BANKS FOR RESEARCH IN THE FIELD OF SPACE BIOLOGY AND MEDICINE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
No 2, 1980 pp 89-90

[Article* by V. V. Verigo and Yu. G. Korotenkov, submitted 29 Jun 78]

[Text] At the present time, it becomes necessary to store, sort and process a large volume of data in solving many medical and biological problems. Data banks (DB) which are organized on computers are used for this purpose. Efficient construction and use of DB is possible provided both mathematicians and consumers--medical workers, for whom it is quite useful to learn about the principles of organizing DB and use of information obtained from them, work together.

A BD is a complex of software which includes a data base (data storage) and a system to control it: an aggregate of programs and hardware for access to data and processing thereof. A detailed description of DB organization was published previously [1-4].

In order to request entries in the DB one uses coded designations, i.e., identifiers. Information inputted from a group of consumers is usually interrelated, and the identifier for each entry is logically broken down into several hierarchic levels. In our opinion, most of the requirements of DB for the needs of space medicine and biology can be met by using a hierarchic tree structure of DB [2, 3].

The first important function of DB is work as an information and reference system, i.e., storing data in the form of separate entries, entering them according to identifiers that are broken down into levels reflecting the content of each concrete reference and relation between different references, retrieval of references by title and entering these references in the DB consumer's array. The consumer can request a reference on an automatic digital printer, display screen or use it then in his programs.

*R. M. Bayevskiy, Yu. P. Druzhinin (deceased), N. I. Vikhrov and T. D. Semenova participated actively in discussing problems pertaining to development of specialized DB, and the authors wish to express their deep appreciation to them.

The DB can provide additional services, for example, entering a reference in the place of another after processing one that has been read. The DB contains not only references of a textual nature, the operations with which are performed as with constant [unchanging] storage bits, but the results of biomedical measurements, the different elements of which may be combined at the discretion of the consumer.

The DB reference identifier may consist of up to 15 levels. The reference is entered in the form of lines of symbols 80 bytes in length. Accordingly, reading procedures input the reference in the consumer's array in the form of lines of symbols. The DB offers the procedure for converting these lines into a digital array so that the consumer can, if necessary, process the reference or subentry. The consumer may also require the procedure of reverse conversion. Retrieval of an individual entry according to its identifier is a mandatory function of the DB reading procedure. In this case, the request mentions one and only one name for each hierarchic level. It is also possible to issue a group of references as one request. The logic structure of organizing data in one of the DB that has been created involves [implies] chain addressing. In each chain, there are indications for any of its elements not only of the next element in the chain, but the preceding and main element of this chain, which makes it possible to create a reading procedure that is capable of outputting a group of references in response to the most diverse requests. For example, one can include a list of names, rather than only one, in a request for each hierarchic level. For levels selected at random [or arbitrarily], one does not need to indicate the names [titles] at all. A reference satisfies a given request if one of the following conditions is met for each hierarchic level of its identifier: the name of the level corresponds to one of the elements in the list of names in the request for this level; the list of names in the request is blank for this level. With such requests, the reading procedure retrieves all information that satisfies such requests. One can also use another variant of this procedure: lists of names for the levels stated in the request are outputted upon request, rather than references. And the name [title] belongs to the list for the level indicated only when there is at least one reference corresponding to the level of the identifier bearing this name and which satisfies this request. This procedure is convenient when working with displays.

A DB was created for research on heliobiology. Determination of the nature of relations between solar activity and biological phenomena made it necessary, in particular, to examine tens of thousands of of "suspicious" cases with regard to their dependence on magnetospheric perturbances (trauma, cardiovascular accidents with serious consequences, etc.). The tag of each object consisted of a set of eight subtags, such as year, month, day, sex, age, etc. When designing the DB procedures, the tag of an object began to be interpreted as a reference identifier with eight hierarchic levels. A reference was interpreted as the number of objects

conforming with a given tag. The entry procedure according to a specified identifier does not involve input of the reference in the usual sense, but of information concerning it. The number at the address defined by the identifier is increased by one by the input procedure. The procedure of counting objects conforming with the specified tag is an appropriate alteration of the DB reading procedure. All of the "references" that satisfy a given request are found, and from the "reference" found one retrieves the number referring to the number of objects conforming with the tag, corresponding to the identifier of this reference. All these numbers are added, and the sum is issued to the consumer. It is convenient to refer to this DB wit request, to satisfy which there is little time while the number of individual entries is great. For example, several minutes are required to retrieve the number of traumas sustained by women each day of the year, whereas it would have been necessary to spend several hours to retrieve the same data by successively scanning and sorting the list.

Of course, it is possible to combine the above-described DB functions. The reference is formed in such a manner that, at the consumer's request and will, one can retrieve all references that meet this request, the sum of numbers designating the time indicated in the references that satisfy this request, or data of both types.

These examples of DB indicate that there is a wide spectrum of applications for this direction of computer use in medicine, and it permits effective solution of a number of problems of both space medicine and biology, and practical public health.

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